Signal detection of ferric carboxymaltose-induced serious adverse events: Analysis of FAERS and systematic review of case reports

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Objective: To evaluate the safety profile of Ferric Carboxymaltose (FCM) by analyzing serious adverse events (SAEs) reported in the FDA Adverse Event Reporting System (FAERS), with stratification by system organ class (SOC), age, gender, geography, and reporter type. The aim is to identify any emerging safety signals and assess the consistency of reported adverse events with the known safety profile of FCM.

Methodology: A retrospective review of FAERS data was conducted for all adverse event reports associated with FCM from 2008 through March 2024. Data was extracted using the FAERS Open Platform dashboard. Events were categorized by SOC, seriousness, age group, gender, geographical region, and reporter type. Descriptive statistics were used to summarize the frequency and distr,ibution of adverse events.

Results: A total of 7,240 case reports were retrieved. The majority of cases were reported in females (74.1%) and elderly patients (55.5%). The most frequently affected SOCs were General Disorders and Administration Site Conditions (15.6%), Skin and Subcutaneous Tissue Disorders (9.3%), and Nervous System Disorders (9.2%). Serious hypersensitivity reactions, including anaphylaxis, were reported in 521 cases, with 7 fatal outcomes. Overall, 192 fatal events were recorded (2.4% of total events). Most reports originated from healthcare professionals (86.15%) and were evenly distributed between domestic and foreign sources.

Discussion: The adverse events reported for FCM are largely consistent with its known safety profile as outlined in the Summary of Product Characteristics (SmPC). The predominance of female cases may reflect higher exposure due to the prevalence of iron deficiency in women. While serious hypersensitivity reactions were observed, their frequency remains low. No new safety concerns were identified from the FAERS data. Limitations of the FAERS database, including underreporting, incomplete data, and lack of denominator information, were acknowledged.

Conclusion: The review confirms that the safety profile of Ferric Carboxymaltose remains consistent with existing product information. The majority of reported adverse events are expected and non-serious. Continued pharmacovigilance and monitoring are recommended, but no new safety signals were detected that warrant regulatory action.

Abbreviations

ADR	Adverse drug reaction
AE	Adverse event
SmPC	Summary of Product Characteristics
FDA	Food and Drug Administration
DIBD	Developmental International birth date
EEA	European Economic Area
FAERS	FDA adverse events reporting system
FCM	Ferric carboxymaltose
PT	Preferred term
INN	International Nonproprietary Names
SOC	System organ class
US	United States

1. OBJECTIVE

This adverse event summary report provides a comprehensive overview of the safety profile of Ferric carboxymaltose (FCM). The data for the report has been sourced from the FAERS database, focusing in reported adverse events. The report will highlight the most common adverse events associated with FCM usage and analyze them SOC wise further

characterized by seriousness. The data is also analyzed based on geography, gender and age.

Furthermore, systematically summarizing and analyzing all identified Adverse Drug Reactions (ADRs), this report will present a clear and concise overview of the safety profile of FCM.

2. DRUG BACKGROUND

Ferric carboxymaltose received EMA and US Food and Drug Administration (FDA) approval for the treatment of iron deficiency anaemia in adult patients who are intolerant of oral iron or have had an unsatisfactory response to oral iron and in adult patients with or without non-dialysis-dependent chronic kidney disease.

The active pharmaceutical ingredient (API) is available as Injectafer® [marketed under the name of Ferinject ® (Ferric Carboxymaltose)]. The API is Iron (III)-hydroxide carbohydrate complex with a half-life of 7-12 hrs. (Cada DJ et al., 2014).

2.1 INDICATION

Ferric carboxymaltose is indicated for the treatment of iron deficiency under below mentioned conditions:

- oral iron preparations are ineffective.
- oral iron preparations cannot be used.
- there is a clinical need to deliver iron rapidly.

The diagnosis of iron deficiency must be based on laboratory tests.

2.2 Qualitative and Quantitative Composition

- One mL of dispersion contains ferric carboxymaltose corresponding to 50 mg iron.
- Each 2 mL vial contains ferric carboxymaltose corresponding to 100 mg iron.
- Each 10 mL vial contains ferric carboxymaltose corresponding to 500 mg iron.
- Each 20 mL vial contains ferric carboxymaltose corresponding to 1,000 mg iron.

2.3 Safety profile

2.3.1 Adverse Drug Reactions

As per SmPC: Dated 24 Jan 2024, The most commonly reported ADR is nausea (occurring in 3.2% of the subjects), followed by injection/infusion site reactions, hypophosphataemia, headache, flushing, dizziness, and hypertension. The occurrence reported is common (≥ 1/100 to <1/10)

Additionally, Serious hypersensitivity reactions, including anaphylactic-type reactions which can be life-threatening and fatal, have been reported. Patients may present with shock, clinically significant hypotension, loss of consciousness, and collapse. Spontaneous reports from the post-marketing setting, urticaria, dyspnoea, pruritis, tachycardia, erythema, pyrexia, chest discomfort, chills, angioedema, back pain, arthralgia, and syncope have also been reported.

2.3.2 Monitoring

Careful monitoring of the patients for any signs and symptoms of hypersensitivity reactions during and following each administration of FCM is required.

FCM should only be administered when staff trained to evaluate and manage anaphylactic reactions is immediately available, in an environment where full resuscitation facilities can be assured. The patient should be observed for adverse effects for at least 30 minutes following each FCM administration.

2.3.2 Special Warnings

Under the below-mentioned conditions, the administration of FCM should be monitored:

- Hypersensitivity reactions
- Hypophosphataemic osteomalacia
- Hepatic or renal impairment
- Infection
- Extravasation

2.3.4 Contraindications

The use of FCM is contraindicated in cases of:

- hypersensitivity to the active substance, to FCM or any of its excipients
- known serious hypersensitivity to other parenteral iron products.
- anaemia not attributed to iron deficiency, e.g. other microcytic anaemia
- evidence of iron overload or disturbances in the utilization of iron.

3. DATA COLLECTION AND STRATEGY

3.1 DATA SOURCE

Data for this report was retrieved from the FAERS database. The FAERS (FDA Adverse Event Reporting System) database is a repository of adverse event

reports submitted to the U.S. Food and Drug Administration (FDA). It contains information on adverse events, medication errors, and product quality issues associated with various FDA-regulated products such as drugs, biologics, medical devices, dietary supplements, and cosmetics.

A detailed strategy used for retrieval of the data is summarized below in

Table 1

Table 1 Details of the search criteria used for case retrieval.

Criteria	Search Criteria used in this report
Reporting period	Cumulative through 31 March 2024
Database search cut-off date:	August 2025
Report sources:	Spontaneous
Suspect drug(s):	Ferric carboxymaltose
Search engine	FAERS dashboard Open Platform
Notes on search:	All adverse events reported in the FAERS database

4. METHODOLOGY OF ANALYSIS OF DATA

To review the safety profile of Ferric carboxymaltose, the reported adverse events were thoroughly reviewed and documented. This analysis aimed to identify patterns, trends, and potential safety concerns associated with this medication. The data available in various tabs was meticulously reviewed and analyzed in the following categories.

SOCs

A comprehensive assessment was conducted to determine the distribution of adverse events across different system organ classes. The seriousness of these events was also evaluated and presented. A detailed SOC-wise analysis was conducted to identify any specific safety findings which contributed to more than 60% of the total events.

Geographical Distribution

A geographical analysis was conducted to understand the distribution of adverse events in different regions. By examining this data, we were able to identify any potential variations or trends in the occurrence of adverse events based on geographic location.

Gender

The data was further examined to assess if there were any gender-related differences in the reporting of adverse events. This analysis provided valuable insights into potential variations in the occurrence and severity of adverse events between males and females.

Age

To better understand the impact of age on adverse event occurrence, the data was categorized and analyzed according to different age groups. This allowed us to determine if there were any age-specific patterns or trends in the reporting of adverse events.

The components of this ADR summary report include an analysis of the demographic and medical characteristics of ADRs, a summary of the types and frequencies of ADRs observed, a comparison of ADR rates over time, and an assessment of the seriousness and severity of adverse events.

Reporter Type

The data was further examined to assess if there were any reporter-type-related differences in the reporting of adverse events. This analysis provided valuable insights into potential variations in the reporting of AEs which can be further classified as Medically confirmed (by HCPs) and non-medically confirmed (Consumers)

5. RESULTS

Data Overview

A total of 8,229 case reports (Expedited, and Non-expedited) were retrieved with FCM from the FAERS database until August 2025. The details of these cases are categorized based on SOC age, gender, and geography. A data overview of all these cases is presented below in Table 2 and Figure 1.

Table 2 Counts of Cases by Reporting year

Years	Number of Cases	Percentage
2025	535	6.50%
2024	603	7.33%
2023	834	10.13%
2022	886	10.77%
2021	750	9.11%
2020	863	10.49%
2019	1,037	12.60%
2018	870	10.57%
2017	670	8.14%
2016	460	5.59%
2015	402	4.89%
2014	237	2.88%
2013	66	0.80%

2012	7	0.09%
2010	2	0.02%
2009	6	0.07%
2008	1	0.01%
Total	8,229	100.00%

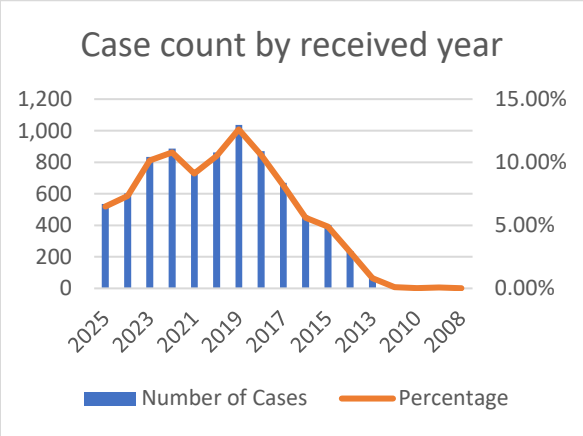

Figure 1 Counts of Cases over reporting years

The count includes various reports including expedited, non-expedited and direct.

- Direct reports are voluntarily submitted to the FDA through the MedWatch program by consumers and healthcare professionals.
- Mandatory reports are submitted by the manufacturer and are categorized as:
  - Expedited reports that contain at least one adverse event that is not currently described in the product labeling and for which the patient outcome is serious, or
  - Non-expedited reports that do not meet the criteria for expedited reports, including cases that are reported as serious and expected, non-serious and unexpected and non-serious and expected.

5.1 DISTRIBUTION OF OVERALL CASES - AGE GROUP

Of the 8,229 cases where the age group was reported, most of the cases are reported from the adult group i.e.18-64 years (n=3,601; 43.76%), followed by the elderly age group i.e.≥65 years (n=1,264; 15.36%). The remaining age group reported less than 5% of cases. Additionally, there were 3,176 cases (38.60%) where no information regarding the age group was reported. The details are presented below

Table **3** and Figure 2.

Table 3 Distribution pattern of cases by age grouping

Category	Number of Cases	Percentage
0-1 Month	33	0.40%
2 Months-2 Years	15	0.18%
3-11 Years	13	0.16%
12-17 Years	127	1.54%
18-64 Years	3,601	43.76%
65-85 Years	1,013	12.31%
More than 85 Years	251	3.05%
Not Specified	3,176	38.60%
Total	8,229	100.00%

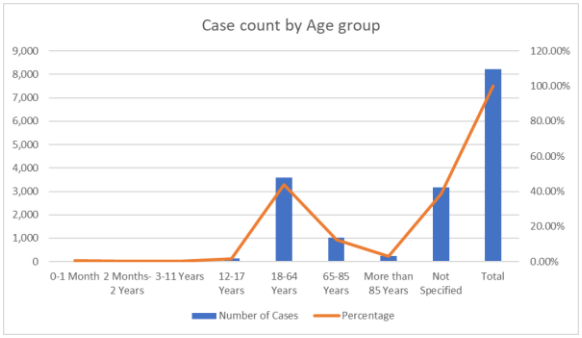

Figure 2 Distribution pattern of cases by age group.

5.2 DISTRIBUTION OF OVERALL CASES – GENDER/SEX

Of the total 8,229 cases, 6,094 (74.06%) were reported in females, 1,228 cases (14.92%) were reported in males, and the remaining 907 cases (11.02%) no information regarding gender was reported. The details are presented in

Table 4 and Figure 3.

Table 4 Distribution pattern of cases by Gender/Sex

Category	Number of Cases	Percentage
Female	6,094	74.06%
Male	1,228	14.92%
Not Specified	902	11.02%
Total	7,240	100.00%

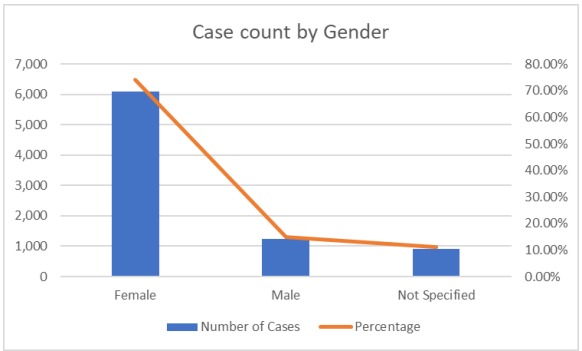

Figure 3 Distribution pattern of cases by Gender/Sex

5.3 DISTRIBUTION OF OVERALL CASES BY OUTCOME

The SOC wise distribution of all fatal cases (patient died) reported are mentioned in the Table below. It is important to note that single case analysis for these cases was not possible because of the limitation of database therefore it doesn't not imply that the death were caused by FCM

The total number of fatal cases reported with FCM is 192 (2.4%). The calculation are done by the number of fatal event reported divided by the total events reported with FCM (n= 9,239) (As the information available takes into account the suspected undesirable effect(s) (adverse reactions) reported in an individual case; as an individual case may refer to more than one suspected undesirable effect and does NOT represent the individual case outcome that have been reported to FAERS, but the number of related undesirable effects). Numbers and percentages are given in the Table 5 and the pattern of outcome reported via reporting years in Figure 4

Table 5 The pattern of all event outcomes

Case Outcome	Counts	Percentage of events
Other Outcomes	4,092	44.29
Non-Serious	2,144	23.21
Hospitalized	1,704	18.44
Life Threatening	561	6.07
Disabled	429	4.64
Died	218	2.36
Required Intervention	61	0.66
Congenital Anomaly	30	0.32
Total	9239	100%

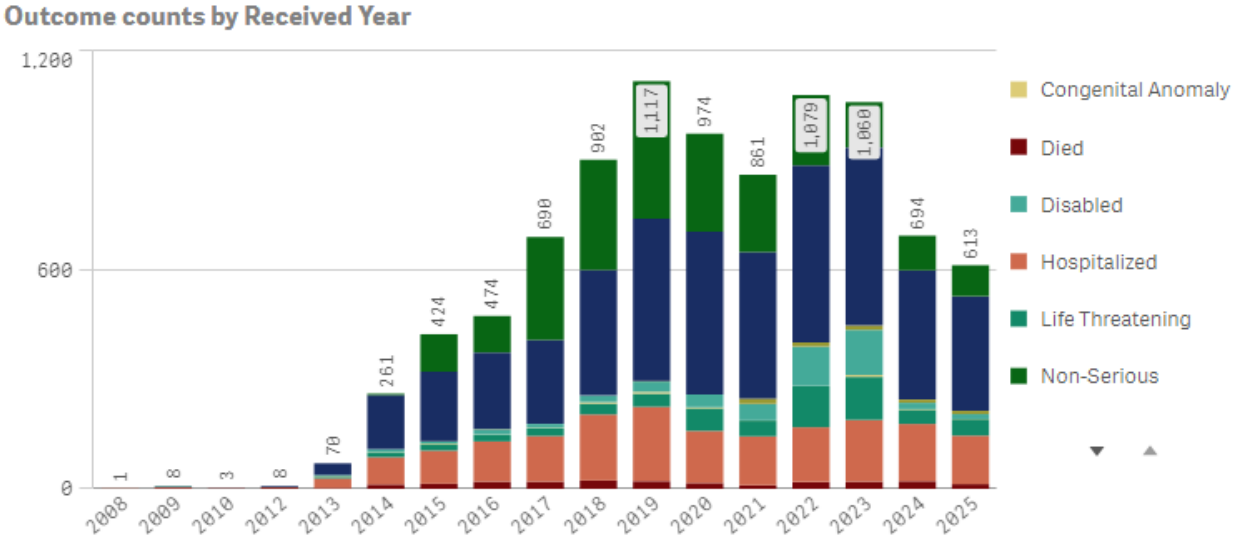

Figure 4 Distribution of event outcome via reporting years

5.4 DISTRIBUTION OF OVERALL CASES – GEOGRAPHY

5.4.1 Domestic/Foreign

Of the 8,229 cases, majority of the cases were medically confirmed i.e. healthcare professional reported (85.6%). The remaining were either reported by consumers (13.23%) or were not specified (1.12%).

The details are presented in Table 6.

Table 6 Distribution of cases in Domestic and Foreign countries

	Reporter Region			
Reaction Group	Number of Cases	Domestic	Foreign	Not Specified
General Disorders and Administration Site Conditions	3,253	1,556	1,697	-
Skin And Subcutaneous Tissue Disorders	1,979	812	1,167	-
Nervous System Disorders	1,924	835	1,089	-
Gastrointestinal Disorders	1,664	814	850	-
Injury, Poisoning and Procedural Complications	1,592	434	1,158	-

Respiratory, Thoracic and Mediastinal Disorders	1,404	540	864	-
Metabolism And Nutrition Disorders	1,256	828	428	-
Musculoskeletal And Connective Tissue Disorders	1,220	667	552	1
Investigations	1,215	566	649	-
Vascular Disorders	1,080	349	731	-
Cardiac Disorders	786	227	559	-
Psychiatric Disorders	578	355	223	-
Immune System Disorders	567	220	347	-
Product Issues	394	323	71	-
Infections And Infestations	311	48	263	-
Pregnancy, Puerperium and Perinatal Conditions	263	12	251	-
Eye Disorders	204	59	145	-
Renal And Urinary Disorders	191	40	151	-
Blood And Lymphatic System Disorders	189	23	166	-
Hepatobiliary Disorders	160	9	151	-
Social Circumstances	140	97	42	1
Ear And Labyrinth Disorders	130	41	89	-
Surgical And Medical Procedures	110	24	86	-
Reproductive System and Breast Disorders	71	29	42	-
Congenital, Familial and Genetic Disorders	53	2	51	-
Endocrine Disorders	52	10	42	-
Neoplasms Benign, Malignant and Unspecified (Incl Cysts And Polyps)	50	10	39	1
Total Cases	8,229	4,033	4,194	2

5.4.2 Distribution via Reporter Type

From the total 8,229 cases, most of the cases were medically confirmed by Healthcare professional (85.65%). The remaining were either reported by consumers (13.23%) or were not specified (1.12%). The detail of the reporter type is presented in Figure 5 and Table 7

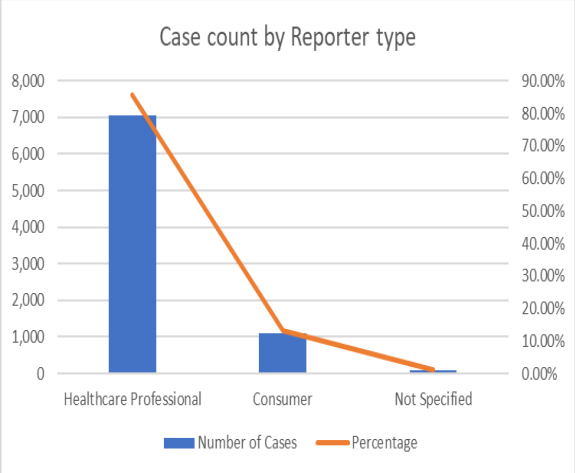

Figure 5 Distribution pattern of cases by Reporter type

Table 7 Distribution of cases by reporter type

Category	Number of Cases	Percentage
Healthcare Professional	7,048	85.65%
Consumer	1,089	13.23%
Not Specified	92	1.12%
Totals	8,229	100.00%

5.5 DISTRIBUTION OF OVERALL CASES – SOC-WISE

The majority of the adverse events were reported from the SOC General disorders and administration site reactions followed by skin and subcutaneous tissue disorders, Nervous system disorders, Gastrointestinal disorders, Injury, Poisoning and Procedural Complications, Respiratory, thoracic and mediastinal disorders, Metabolism and Nutrition Disorders, Musculoskeletal and Connective Tissue Disorders, and Investigations. The details of the remaining SOCs and their stratification are presented in

Table **8**

Table 8 Distribution of Cases via SOC

SOC	Count of Cases
General Disorders and Administration Site Conditions	3,253
Skin And Subcutaneous Tissue Disorders	1,979
Nervous System Disorders	1,924
Gastrointestinal Disorders	1,664
Injury, Poisoning and Procedural Complications	1,592
Respiratory, Thoracic and Mediastinal Disorders	1,404
Metabolism And Nutrition Disorders	1,256
Musculoskeletal And Connective Tissue Disorders	1,220
Investigations	1,215
Vascular Disorders	1,080
Cardiac Disorders	786
Psychiatric Disorders	578
Immune System Disorders	567
Product Issues	394
Infections And Infestations	311
Pregnancy, Puerperium and Perinatal Conditions	263
Eye Disorders	204
Renal And Urinary Disorders	191
Blood And Lymphatic System Disorders	189
Hepatobiliary Disorders	160
Social Circumstances	140
Ear And Labyrinth Disorders	130
Surgical And Medical Procedures	110
Reproductive System and Breast Disorders	71
Congenital, Familial and Genetic Disorders	53
Endocrine Disorders	52
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	50

Table 9 Distribution of Cases via SOC and Age group

		Age Group							
Reaction Group	Number of Cases	0-1 Month	2 Months -2 Years	3-11 Years	12-17 Years	18-64 Years	65-85 Years	More than 85 Years	Not Specified
Total Cases	8,229	33	15	13	127	3,601	1,013	251	3,176
General Disorders and Administration Site Conditions	3,253	6	7	4	55	1,625	343	89	1,124
Skin And Subcutaneous Tissue Disorders	1,979	1	3	6	45	1,097	208	33	586
Nervous System Disorders	1,924	6	7	2	29	1,051	201	59	569
Gastrointestinal Disorders	1,664	2	-	2	32	868	197	47	516
Injury, Poisoning and Procedural Complications	1,592	31	13	7	46	866	127	34	468
Respiratory, Thoracic and Mediastinal Disorders	1,404	9	4	2	26	763	185	47	368
Metabolism And Nutrition Disorders	1,256	3	-	2	12	525	137	31	546
Musculoskeletal And Connective Tissue Disorders	1,220	2	2	-	20	658	112	14	412
Investigations	1,215	3	4	4	12	582	165	47	398
Vascular Disorders	1,080	1	3	2	20	543	162	43	306
Cardiac Disorders	786	7	-	1	13	374	136	46	209
Psychiatric Disorders	578	-	3	-	8	299	43	11	214
Immune System Disorders	567	-	-	-	14	304	68	9	172
Product Issues	394	-	-	1	8	159	25	4	197
Infections And Infestations	311	4	-	-	2	159	52	22	72
Pregnancy, Puerperium And Perinatal Conditions	263	17	7	-	1	120	-	-	118
Eye Disorders	204	1	-	1	9	128	17	2	46
Renal And Urinary Disorders	191	1	1	-	1	105	36	13	34
Blood And Lymphatic System Disorders	189	2	-	-	4	85	38	14	46
Hepatobiliary Disorders	160	2	1	-	-	58	53	12	34
Social Circumstances	140	-	-	-	1	65	21	1	52
Ear And Labyrinth Disorders	130	2	-	-	1	99	5	-	23
Surgical and Medical Procedures	110	3	-	-	1	49	9	3	45
Reproductive System and Breast Disorders	71	-	-	-	-	47	3	-	21
Congenital, Familial and Genetic Disorders	53	9	5	-	-	19	-	-	20

Endocrine Disorders	52	-	-	-	-	37	4	3	8
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	50	-	-	-	-	14	14	2	20

Of note: The count may not match up with the total number of cases as 1 case may be reporting multiple adverse events.

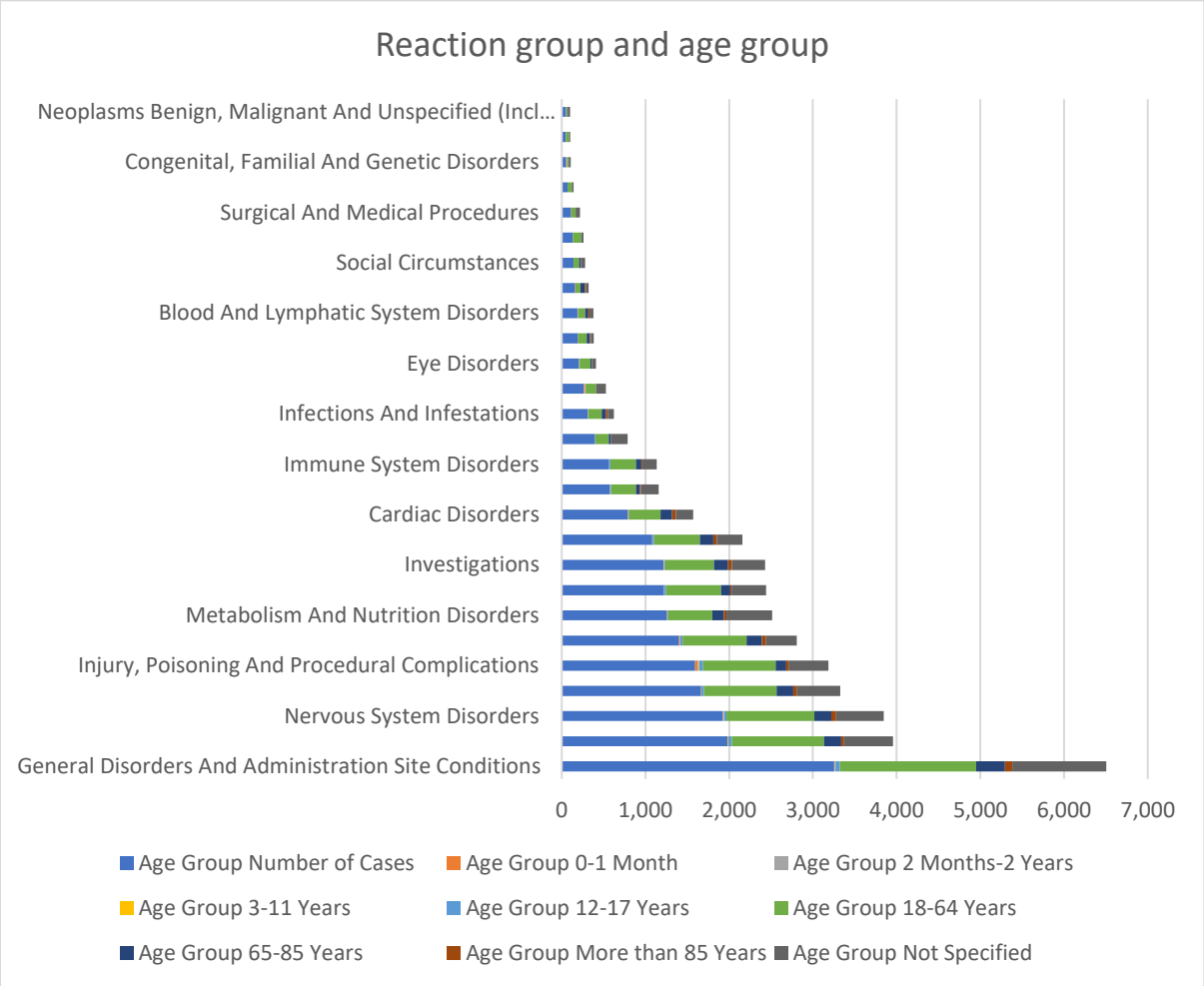

Figure 6 Distribution of Cases by SOC

These cases were further reviewed to see the seriousness trends which are presented below in **Error! Reference source not found.**. The trends reported in regard were similar to the overall SOC trends. The maximum number of serious events were reported in the SOC General disorders and administration site reactions followed by Skin and subcutaneous tissue disorders and Nervous system disorders.

5.5.1 Distribution of SOC via Gender/Sex

The pattern of distribution of events is similar to overall counts stratified by gender, where majority of the cases are reported in females (n=5365; 74.1%) than male (n=1063; 14.6%). There were 11.2% cases where no information by gender/sex was reported. Refer to

Table **10** for details.

Table 10 The pattern of distribution of SOC via Gender/Sex

Reaction Group	Number of Cases	Female	Male	Not Specified
Total Cases	7,240	5,365	1,063	812
General Disorders and Administration Site Conditions	2,894	2,277	378	239
Skin And Subcutaneous Tissue Disorders	1,712	1,404	179	129
Nervous System Disorders	1,700	1,391	208	101
Gastrointestinal Disorders	1,512	1,213	175	124
Injury, Poisoning and Procedural Complications	1,391	1,119	186	86
Respiratory, Thoracic and Mediastinal Disorders	1,242	973	183	86
Musculoskeletal And Connective Tissue Disorders	1,130	928	142	60
Metabolism And Nutrition Disorders	1,106	844	165	97
Investigations	1,053	768	177	108
Vascular Disorders	956	724	147	85
Cardiac Disorders	704	543	122	39
Psychiatric Disorders	526	471	47	8
Immune System Disorders	503	374	70	59
Product Issues	374	333	28	13
Infections And Infestations	280	193	68	19
Pregnancy, Puerperium and Perinatal Conditions	234	191	23	20
Eye Disorders	183	152	21	10
Blood And Lymphatic System Disorders	169	108	53	8
Renal And Urinary Disorders	162	111	43	8
Social Circumstances	132	110	22	-
Ear And Labyrinth Disorders	122	113	8	1
Hepatobiliary Disorders	121	80	31	10
Surgical And Medical Procedures	93	72	15	6
Reproductive System and Breast Disorders	65	62	2	1
Endocrine Disorders	48	39	8	1
Neoplasms Benign, Malignant and Unspecified (Incl Cysts and Polyps)	44	21	20	3
Congenital, Familial And Genetic Disorders	42	30	9	3

6. THE PATTERN OF DISTRIBUTION OF CASES PER SOCS CONTRIBUTING TO THE MAJORITY OF THE CASES

6.1 GENERAL DISORDERS AND ADMINISTRATION SITE REACTIONS

In this SOC, most cases reported the adverse event of fatigue, malaise, asthenia, followed by fatigue and chest pain which accounts for the majority of the total cases. The remaining events were reported with less than 10% frequency. The total fatal events account for 2.9% of the total events under SOC. The pattern of Adverse event (AE) reporting, event outcome, and age group in these cases is reported in below mentioned Table 11.

Table 11 The pattern of AE reporting in General disorders and administration site reactions

Preferred Term	Number Of Individual Cases
Pain	511

Malaise	380
Fatigue	331
Asthenia	329
Pyrexia	326
Chest Pain	314
Chest Discomfort	276
Chills	173
Influenza Like Illness	134
Ill-Defined Disorder	121
Infusion Site Extravasation	117
Feeling Hot	112
Infusion Site Discolouration	109

Interpretation of results: Most of the cases reported were pain, malaise, asthenia, fatigue, chest pain, pyrexia, chest discomfort, and administration site reactions/Infusion site reactions (including discolouration, bruising, pain etc.), influenza like illness which are within the known safety profile of the drug (SmPC). No other specific pattern was observed for the remaining AEs/PTs.

6.2 Skin and Subcutaneous Tissue Disorders

In this SOC, most cases reported adverse events were urticaria, pruritus, rash, and erythema, which accounts for majority of the cases. All other events were reported with less than 10% frequency. The total fatal events account for 0.5% of the total events under SOC. The pattern of AE reporting and event outcome in these cases is reported in below mentioned Table 12.

Table 12 Pattern of AE reporting in Skin and subcutaneous tissue disorders

Preferred term	Number of Individual cases
Pruritus	533
Urticaria	522
Rash	379
Erythema	221
Skin Discolouration	216
Hyperhidrosis	147
Angioedema	80
Rash Pruritic	65

Interpretation of results: The majority of the cases included pruritus, urticaria, rash, erythema, skin discolouration, hyperhidrosis, angioedema and rash pruritic, etc. which are known adverse events with the drug (SmPC). No specific pattern was observed for the remaining AEs/PTs.

6.3 Nervous System Disorders

In this SOC, the majority of the cases reported headache, dizziness, and paraesthesia which accounts for the majority of the cases. The remaining events were reported with less than 10% frequency. The total fatal events account for 1.7% of the total events under SOC. The pattern of AE reporting and event outcome in these cases is reported in below mentioned Table 13.

Table 13 Pattern of AE reporting in Nervous system disorders

Preferred term	Number of Individual cases
Headache	608
Dizziness	531
Paraesthesia	201
Loss of consciousness	166
Hypoaesthesia	111
Syncope	104
Tremor	91

Interpretation of results: Most of the cases reported included loss of consciousness, vertigo, paraesthesia (hypo and hyper), headache and dizziness which are within the known safety profile of the drug (SmPC). No specific pattern was observed for the remaining AEs/PTs.

6.4 GASTROINTESTINAL DISORDERS

In this SOC, the majority of the cases reported were nausea, vomiting, abdominal pain, and diarrhoea which accounts for the majority of the cases. The remaining events were reported with less than 10% frequency. The total fatal events account for 0.59% of the total events. The pattern of AE reporting and event outcome in these cases is reported in below mentioned Table 14.

Table 14 Pattern of AE reporting in Gastrointestinal disorders

Preferred term	Number of Individual cases
Nausea	888
Vomiting	403
Abdominal Pain	221
Diarrhoea	182
Abdominal pain upper	105

Interpretation of results: Most of the cases reported included nausea, vomiting, abdominal pain, and

diarrhoea, bloating, flatulence, which are within the known safety profile of the drug (SmPC). No specific pattern was observed for the remaining AEs/PTs.

6.5 INJURY, POISONING AND PROCEDURAL COMPLICATIONS

In this SOC, the majority of cases reported Maternal Exposure During Pregnancy, Infusion Related Reaction, Off Label Use, Exposure During Pregnancy, Foetal Exposure During Pregnancy and Product Use in Unapproved Indication accounts for the majority of the cases. The total fatal events account for 2.6% of the total events under SOC. The pattern of AE reporting and event outcome in these cases is reported in below mentioned Table 15.

Table 15 Pattern of AE reporting in Immune system disorder

Preferred term	Number of Individual cases
Maternal Exposure During Pregnancy	465
Infusion Related Reaction	170
Off Label Use	156
Exposure During Pregnancy	139
Foetal Exposure During Pregnancy	107
Product Use in Unapproved Indication	92

Interpretation of results: Most of the cases reported were Hypersensitivity, Anaphylactic reaction, Anaphylactoid reaction, Type I hypersensitivity, and Anaphylactic shock, which is aligned with safety profile of FCM Hypersensitivity reactions are presented and well defined in the warning and precaution section of the (SmPC). No specific pattern was observed for the remaining AEs/PTs.

7. DISCUSSION AND CONCLUSION

FCM is an intravenous iron replacement therapy used to treat iron deficiency anaemia when oral iron is ineffective or cannot be utilized. Here is an overview of the safety profile of FCM based on clinical trials and post-marketing surveillance data:

- Common Adverse Events: The most commonly reported adverse events include transient hypophosphatemia (low phosphate levels), dizziness, nausea, headache, and vomiting.
- Hypersensitivity Reactions: Infusion-related hypersensitivity reactions, including anaphylaxis, have been reported with the use of FCM. These reactions are rare but potentially severe. Therefore, FCM should be administered under appropriate medical supervision with access to resuscitation equipment.
- Delayed Hypersensitivity Reactions: Delayed hypersensitivity reactions with FCM have been reported, typically occurring several days after administration. Symptoms such as rash, fever, joint pain, and lymphadenopathy should be promptly evaluated and managed if they occur.
- Cardiovascular Safety: Clinical trials and post-marketing surveillance data have not shown an increased risk of major adverse cardiovascular events with FCM use. However, FCM should be used with caution in patients with a history of cardiovascular disease.
- Tolerance: FCM has shown good tolerability even in patients with comorbidities or other medical conditions. It can be used in patients with chronic kidney disease, inflammatory bowel disease, and other underlying conditions.
- Fatal events: A low proportion of fatal events were seen in the SOCs presenting the majority of the events. No specific concerns regarding SAEs leading to death were noted.

Monitoring: Regular monitoring of vital signs, including blood pressure, should be performed during FCM administration. Monitoring for signs of hypersensitivity reactions or other adverse events is also crucial.

From the review of available data from the FAERS database, it can be concluded that the majority of the cases are reported in the adult age group and the maximum cases reported from France. The adverse events are reported more in females as compared to males which could be because of the more exposure of females to FCM because of the iron deficiency in females (Alvarez-Uria G et al., 2014; Le CH., 2016).

In terms of safety profile, the majority of the cases were reported from general disorders and administration site reactions followed by skin and subcutaneous tissue disorders. Of note all the events reported for these SOCs were within the known safety profile of the drug as per product SmPC. Overall, the

pattern of AEs reporting was found to be in line with the findings from the EudraVigilance database Therefore, after the review of the database cases no new safety concern is identified.

Of note the open FAERS database has certain limitations that should be taken into consideration when analyzing adverse event and are summarized below: -

- Underreporting: Adverse events are voluntarily reported to FAERS, and it is estimated that only a small fraction of actual events are reported. This can lead to an underrepresentation of the true frequency and severity of adverse events for a particular product.
- Incomplete Information: The information provided in FAERS reports can be incomplete or include limited details about the adverse event, the patient, or the circumstances surrounding the event. This can make it challenging to fully assess the clinical context and causality of the reported event.
- Reporting Bias: The data in FAERS can be subject to reporting bias, as certain events may be more likely to be reported than others. Factors such as media attention, recent label changes, or marketing efforts can influence reporting patterns, leading to over- or under-representation of particular adverse events.
- Duplicate Reports: FAERS may contain duplicate reports of the same adverse event, which can affect the accuracy of data analysis and lead to overestimation of event frequencies.
- Lack of Denominator Data: FAERS provides information about adverse events but does not include information on the denominator (the number of people exposed to a particular product). Without this information, it is difficult to determine the true incidence or prevalence of adverse events.
- Misclassification and Data Quality: The quality and accuracy of the data in FAERS rely on the reporting sources, which can vary in terms of the level of expertise and adherence to reporting guidelines. Misclassification of events or errors in the data entry process can impact the reliability of the database.
- Confounding Factors: FAERS data does not typically include detailed patient-level information, such as confounding factors or underlying medical conditions, which can complicate the analysis and interpretation of adverse events.

Considering these limitations, FAERS data should be interpreted cautiously and used as part of a comprehensive approach to drug safety evaluation, including other sources of data such as clinical trials, observational studies, and systematic reviews.

Additional data sources can supplement the analysis and methodologies to obtain a more accurate understanding of drug safety profile.

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