# SAFETY DATA SHEET

## SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

**Contact information**

**General**

Celgene Corporation
86 Morris Avenue, Summit, NJ 07901
Main: +1 (908) 673-9000
E-mail: MSDScoordinator@Celgene.com

**Emergency telephone number**

Chemtrec *(24-hour availability)*:
+1 (800) 424-9300 (USA and Canada)
+1 (703) 527-3887 (International; collect calls accepted)

**Product identifier**

Inrebic Capsules, 100 mg

**Synonyms**

Fedratinib Capsules, 100 mg;
Containing 100-mg fedratinib free base (equivalent to 117.3 mg fedratinib dihydrochloride monohydrate) per capsule

**Trade names**

Inrebic™ [Serial Number: 86690908; Registration Number: 4931750]

**Chemical family**

Mixture - contains a sulfonamide

**Relevant identified uses of the substance or mixture and uses advised against**

Bulk formulated pharmaceutical mixture/Formulated pharmaceutical product/ mixture packaged in final form for patient use; indicated for the treatment of cancer.

**Note**

This SDS is written to address potential worker health and safety issues associated with the handling of the formulated drug product.

## SECTION 2 - HAZARDS IDENTIFICATION

**Classification of the substance or mixture**

**Drugs in the finished state and intended for the final user are not subject to labeling in the US, EU or Canada.** Please consult the prescribing/packaging information. **The classification and labelling listed below is for bulk drug product.**

## SECTION 2 - HAZARDS IDENTIFICATION …continued

**Globally Harmonized System [GHS]**

Reproductive Toxicity - Category 2. Specific Target Organ Toxicity (repeated exposure) - Category 1.

### Label elements

**GHS hazard pictogram**

**GHS signal word**

Danger

**GHS hazard statements**

H361d - Suspected of damaging the unborn child. H372 - Causes damage to lymphatic system, bone marrow, liver, heart, skeletal muscle, and lungs through prolonged or repeated exposure.

**GHS precautionary statements**

P201 - Obtain special instructions before use. P202 - Do not handle until all safety precautions have been read and understood. P260 - Do not breathe dust. P264 - Wash hands thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P281 - Use personal protective equipment as required. P308 + P313 - IF exposed or concerned: get medical advice/attention. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/ regional/national/international regulations.

**Other hazards**

Fedratinib is a Janus Associated Kinase 2 (JAK2) and fibromyalgia syndrome (FMS)-like receptor tyrosine kinase 3 (FLT3) inhibitor. In clinical trials, the most commonly reported adverse effects in healthy volunteers included mild gastrointestinal (GI) disorders (diarrhea, nausea, vomiting). Similar GI effects, clinical chemistry changes, decreased blood cell counts (red blood cell counts and platelets), and encephalopathy, which were sometimes serious and/or fatal, were frequently noted in patients with myelofibrosis.

**Note**

This product/mixture is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

## SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

| Ingredient | CAS # | EINECS/ ELINCS# | Amount | GHS Classification |
|---|---|---|---|---|
| Microcrystalline Cellulose | 9004-34-6 | N/A | 50-60%* | Not classified |
| Fedratinib dihydrochloride monohydrate | 1374744-69-0 | N/A | 35-40% | RT2: H361d; STOT-R1: H372 |
| Sodium stearyl fumarate | 4070-80-8 | N/A | 1% | SI2: H315; EI2: H319 |

## SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS …continued

| | |
|---|---|
| **Note** | The ingredients listed above are considered hazardous. The remaining components are non-hazardous and/or present at amounts below reportable limits. See Section 16 for full text of GHS classifications.<br><br>*Microcrystalline cellulose, present as a silicified microcrystalline cellulose (SMCC), is listed because it has OELs and is present at or above 1%. |

## SECTION 4 - FIRST AID MEASURES

**Description of first aid measures**

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|---|---|
| **Immediate Medical Attention Needed** | Yes |
| **Eye Contact** | If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor. |
| **Skin Contact** | Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor. |
| **Inhalation** | Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor. |
| **Ingestion** | If swallowed, call a physician immediately. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor. |
| **Protection of first aid responders** | See Section 8 for Exposure Controls/Personal Protection recommendations. |
| **Most important symptoms and effects, both acute and delayed** | See Sections 2 and 11 |
| **Indication of immediate medical attention and special treatment needed, if necessary** | Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively. |

## SECTION 5 - FIREFIGHTING MEASURES

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|---|---|
| **Extinguishing media** | Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials. |

## SECTION 5 - FIREFIGHTING MEASURES …continued

| | |
|---|---|
| **Specific hazards arising from the substance or mixture** | No information identified. May emit carbon monoxide, carbon dioxide, oxides of nitrogen, chlorine-containing compounds, and sulfur-containing compounds. |
| **Flammability/ Explosivity** | No explosivity or flammability data identified. If capsules are crushed or broken, high concentrations of finely divided airborne organic particles can potentially explode if ignited. |
| **Advice for firefighters** | In case of fire in the surroundings: use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use. |

## SECTION 6 - ACCIDENTAL RELEASE MEASURES

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|---|---|
| **Personal precautions, protective equipment and emergency procedures** | If capsules are opened/crushed/broken, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Area should be adequately ventilated. |
| **Environmental precautions** | Do not empty into drains. Avoid release to the environment. |
| **Methods and material for containment and cleaning up** | If capsules are spilled, scoop up and dispose of in a manner that is compliant with federal, state or local laws. If tablets are broken or crushed, DO NOT RAISE DUST. Surround spill or powder with absorbents and place a damp cloth or towel over the area to minimize entry of powder into the air. Add excess liquid to allow the material to enter into solution. Capture remaining liquid onto spill absorbents. Place spill materials into a leak-proof container for disposal in accordance with applicable waste disposal regulations (see section 13). Decontaminate the area twice with an appropriate solvent. |
| **Reference to other sections** | See Sections 8 and 13 for more information. |

## SECTION 7 - HANDLING AND STORAGE

| | |
|---|---|
| **Precautions for safe handling** | Follow recommendations for handling pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Avoid contact with eyes, skin and other mucous membranes. Wash thoroughly after handling. Avoid breathing dust. |
| **Conditions for safe storage including any incompatibilities** | Inrebic Capsules contain 100 mg of fedratinib (free base equivalent) and are packaged in HDPE bottles.<br><br>Store at room temperature ≤ 25°C, away from incompatible materials. Avoid extreme temperatures. |
| **Specific end use(s)** | No information identified. |

## SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

**Control Parameters/ Occupational Exposure Limit Values**

| Compound | Issuer | Type | OEL |
|---|---|---|---|
| Microcrystalline Cellulose | OSHA | REL-TWA | 10 mg/m³ (total); 5 mg/ m³ (respirable) |
| | ACGIH | TLV | 10 mg/m³ |
| | Netherlands | MAC-TGG | 2 mg/m³ |
| | France | VME | 10 mg/m³ |
| Fedratinib dihydrochloride monohydrate | Celgene | OEL | 80 µg/m³ (free base) |
| Sodium stearyl fumarate | -- | -- | -- |

**Exposure/Engineering controls**

None required for normal handling of packaged product. If handling bulk product and/or capsules are opened/crushed/broken: Control exposures to below the OEL (for the active ingredient(s) if available). Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Use engineered local exhaust ventilation (LEV) and/or enclosure at dust generating points and for high dust generating operations such as weighing, material transfers and where energy is used (*e.g.*, milling).

**Respiratory protection**

None required for normal handling of packaged product. If handling bulk product and/or capsules are opened/crushed/broken: Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. At a minimum, a tight-fitting full-face respirator with HEPA filters is required when performing dust or aerosol generating operations. A powered air-purifying respirator (PAPR) with HEPA filters and head cover is required for spill cleanup.

**Hand protection**

None required for normal handling of packaged product. If handling bulk product and/or capsules are opened/crushed/broken: Wear nitrile or other impervious gloves if skin contact is possible. When the material is dissolved or suspended in an organic solvent, wear gloves that provide protection against the solvent.

**Skin protection**

None required for normal handling of packaged product. If handling bulk product and/or capsules are opened/crushed/broken: Wear appropriate gloves, lab coat, or other protective overgarment if skin contact is likely. Base the choice of skin protection on the job activity, potential for skin contact and solvents and reagents in use.

**Eye/face protection**

None required for normal handling of packaged product. If handling bulk product and/or capsules are opened/crushed/broken: Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.

**Environmental Exposure Controls**

Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.

## SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

| | |
|---|---|
| **Other protective measures** | Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors). Decontaminate all protective equipment following use. |

## SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

**Information on basic physical and chemical properties**

| | |
|---|---|
| **Appearance** | Hard Capsule |
| **Color** | Reddish brown opaque size 0 hard gelatin capsule imprinted with white ink |
| **Odor** | No information identified. |
| **Odor threshold** | No information identified. |
| **pH** | No information identified. |
| **Melting point/ freezing point** | No information identified. |
| **Initial boiling point and boiling range** | Not applicable. |
| **Flash point** | No information identified. |
| **Evaporation rate** | No information identified. |
| **Flammability (solid, gas)** | No information identified. |
| **Upper/lower flammability or explosive limits** | No information identified. |
| **Vapor pressure** | No information identified |
| **Vapor density** | No information identified. |
| **Relative density** | No information identified. |
| **Water solubility** | No information identified. |
| **Solvent solubility** | No information identified. |
| **Partition coefficient (*n-octanol/water*)** | No information identified. |
| **Auto-ignition temperature** | No information identified. |

## SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

| | |
|---|---|
| **Decomposition temperature** | No information identified. |
| **Viscosity** | No information identified. |
| **Explosive properties** | No information identified. |
| **Oxidizing properties** | No information identified. |

**Other information**

| | |
|---|---|
| **Molecular formula** | Not applicable (Mixture) |
| **Molecular weight** | Not applicable (Mixture) |

## SECTION 10 - STABILITY AND REACTIVITY

| | |
|---|---|
| **Reactivity** | No information identified. |
| **Chemical stability** | No information identified. |
| **Possibility of hazardous reactions** | No information identified. |
| **Conditions to avoid** | No information identified. |
| **Incompatible materials** | No information identified. |
| **Hazardous decomposition products** | No information identified. |

## SECTION 11 - TOXICOLOGICAL INFORMATION

**Information on toxicological effects**

**Route of entry** May be absorbed by inhalation, skin contact and ingestion.

**Acute toxicity**

| Compound | Type | Route | Species | Dose |
|---|---|---|---|---|
| Microcrystalline Cellulose | $LD_{50}$ | Oral | Rat | >5 g/kg |
| | $LC_{50}$ (4 hour) | Inhalation | Rat | >5800 mg/m$^3$ |
| | $LD_{50}$ | Dermal | Rabbit | > 2 g/kg |
| Fedratinib dihydrochloride monohydrate | -- | -- | -- | -- |
| Sodium stearyl fumarate | -- | -- | -- | -- |

**Irritation/Corrosion** No studies identified for fedratinib. Sodium stearyl fumarate was irritating to rabbit skin and eyes.

**Sensitization** No studies identified.

## SECTION 11 - TOXICOLOGICAL INFORMATION …continued

| | |
|---|---|
| **STOT-single exposure** | No studies identified. |
| **STOT-repeated exposure/Repeat-dose toxicity** | In a 6-month study in rats, oral doses of fedratinib ≥10 mg/kg/day resulted in microscopic changes in lymphatic tissue, bone marrow, liver, forestomach, heart, skeletal muscle, and lungs (NOAEL = 3 mg/kg/day).<br><br>In a 9-month study in dogs, oral doses of fedratinib at 20/15 mg/kg/day resulted in mortality, and effects in the bone marrow, liver, and testes were observed at ≥6 mg/kg/day (NOAEL = 2 mg/kg/day). |
| **Reproductive toxicity** | No adverse effect on fertility or reproductive performance was observed in rats orally administered fedratinib at up to 30 mg/kg/day (considered the NOAEL). |
| **Developmental toxicity** | Postimplantation loss, lower fetal body weights, and skeletal effects were observed in an embryofetal study in rats in the presence of maternal toxicity at oral doses of 30 mg/kg/day. No developmental toxicity was observed in rabbits orally administered fedratinib at up to 30 mg/kg/day during gestation (considered the NOAEL). |
| **Genotoxicity** | Fedratinib was negative in an Ames bacterial mutagenicity assay, an *in vitro* chromosomal aberration assay in Chinese hamster ovary cells, and an *in vivo* rat micronucleus test. |
| **Carcinogenicity** | Fedratinib was not carcinogenic in a 26-week study in transgenic mice at oral doses up to 30 mg/kg/day. The ingredients in this mixture are not listed by NTP, IARC, ACGIH or OSHA as a carcinogen. |
| **Aspiration hazard** | No data available. |
| **Human health data** | See "Section 2 - Other Hazards" |

## SECTION 12 - ECOLOGICAL INFORMATION

**Toxicity**

| Compound | Type | Species | Concentration |
|---|---|---|---|
| Microcrystalline Cellulose | -- | -- | -- |
| Fedratinib dihydrochloride monohydrate | -- | -- | -- |
| Sodium stearyl fumarate | -- | -- | -- |

| | |
|---|---|
| **Persistence and Degradability** | No data available. |
| **Bioaccumulative potential** | No data available. |
| **Mobility in soil** | No data available. |
| **Results of PBT and vPvB assessment** | No data available. |

## SECTION 12 - ECOLOGICAL INFORMATION …continued

| | |
|---|---|
| **Other adverse effects** | No data available. |
| **Note** | The environmental characteristics of this product/mixture have not been fully investigated. Releases to the environment should be avoided. |

## SECTION 13 - DISPOSAL CONSIDERATIONS

| | |
|---|---|
| **Waste treatment methods** | Dispose of wastes by appropriately permitted chemical waste incinerator in accordance to prescribed federal, state, and local guidelines. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, *e.g.*, appropriately permitted municipal or onsite wastewater treatment facility. |

## SECTION 14 - TRANSPORT INFORMATION

| | |
|---|---|
| **Transport** | Based on the available data, this product/mixture is not regulated as a hazardous material/dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG. |
| **UN number** | None assigned. |
| **UN proper shipping name** | None assigned. |
| **Transport hazard classes and packing group** | None assigned. |
| **Environmental hazards** | Based on the available data, this product/mixture is not regulated as an environmental hazard or a marine pollutant. |
| **Special precautions for users** | Due to lack of data, avoid release to the environment. |
| **Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code** | Not applicable. |

## SECTION 15 - REGULATORY INFORMATION

| | |
|---|---|
| **Safety, health and environmental regulations/legislation specific for the substance or mixture** | This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information. |

## SECTION 15 - REGULATORY INFORMATION …continued

| | |
|---|---|
| **Chemical safety assessment** | Not conducted. |
| **TSCA status** | Drugs are exempt from TSCA. |
| **SARA section 313** | Not listed. |
| **California proposition 65** | Not listed. |
| **Additional information** | No other information identified. |

## SECTION 16 - OTHER INFORMATION

| | |
|---|---|
| **Full text of H phrases and GHS classifications** | SI2 - Skin irritant Category 2. H315 - Causes skin irritation. EI2 - Eye irritant Category 2. H319 - Causes serious eye irritation. RT2 - Reproductive toxicity Category 2. H361d - Suspected of damaging the unborn child. STOT-R1 - Specific Target Organ Toxicity Following Repeat Exposure Category 1. H372 - Causes damage to lymphatic system, bone marrow, liver, heart, skeletal muscle, and lungs through prolonged or repeated exposure. |
| **Sources of data** | Information from published literature and internal company data. |
| **Abbreviations** | ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PBT - Persistent, Bioaccumulative, and Toxic; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System |
| **Issue Date** | 8 April 2020 |
| **Revisions** | Updated adverse effects in Section 2; Updated OEL in Section 8; Updated repeat-dose, developmental, and carcinogenicity data in Section 11. |

**Disclaimer**

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.