Prescribing Information

Accofil (filgrastim) 30 MU/0.5 ml, 48 MU/0.5 ml solution for injection or infusion in pre-filled syringe

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Each pre-filled syringe contains 30MU or 48MU (equivalent to 300mcg or 480mcg filgrastim respectively) in 0.5ml solution for injection or infusion.

Indications: Reduction in duration of neutropenia and incidence of febrile neutropenia in patients treated with established cytotoxic chemotherapy for malignancy (except chronic myeloid leukaemia and myelodysplastic syndromes). Reduction in duration of neutropenia in patients undergoing myeloablative therapy followed by bone marrow transplantation considered to be at increased risk of prolonged severe neutropenia. Mobilisation of peripheral blood progenitor cells (PBPC). Long term administration in children or adults with severe congenital, cyclic, or idiopathic neutropenia with an absolute neutrophil count (ANC) ≤0.5 x 10^9/L and a history of severe or recurrent infections to increase neutrophil counts and to reduce the incidence and duration of infection-related events. Treatment of persistent neutropenia (ANC ≤ 1.0 x 10^9/L) in patients with advanced HIV infection to reduce the risk of bacterial infections when other options to manage neutropenia are inappropriate.

Dosage and Administration: Established cytotoxic chemotherapy: 0.5 MU/kg/day (5μg/kg/day) SC injection or IV infusion. Do not administer first dose <24 hours following cytotoxic chemotherapy. Continue daily dosing until neutrophil count has recovered to normal range. Premature discontinuation prior to the time of the expected neutrophil nadir is not recommended. Myeloablative therapy followed by bone marrow transplantation: starting dose 1.0 MU/kg/day (10 μg/kg/day) SC or IV infusion. Administer first dose at least 24 hours after cytotoxic chemotherapy and at least 24 hours after bone marrow infusion. When neutrophil nadir is passed, titrate daily dose against neutrophil response. See SmPC for dose titration in relation to neutrophil response. Mobilisation of PBPC in patients undergoing myelosuppressive or myeloablative therapy followed by autologous PBPC transplantation: When used alone, 1.0 MU (10 μg/kg/day) SC infusion or injection for 5-7 consecutive days. Recommended dose of filgrastim for PBPC mobilisation after myelosuppressive chemotherapy is 0.5 MU (5μg/kg/day) SC injection given daily from first day after completion of chemotherapy until neutrophil count has recovered to normal range. For PBPC mobilisation in normal donors prior to allogeneic PBPC transplantation: 1.0 MU/kg/day (10 μg/kg/day) SC injection for 4 - 5 consecutive days. Congenital neutropenia: 1.2 MU/kg/day (12 μg/kg/day) SC injection. Idiopathic or cyclic neutropenia: 0.5 MU/kg/day (5 μg/kg/day) SC injection. HIV: Reversal of neutropenia; start 0.1 MU/kg/day (1 μg/kg/day) SC with titration up to a maximum of 0.4 MU/kg/day (4 μg/kg/day) until normal neutrophil count reached and maintained. Maintenance of normal neutrophil counts: the minimal effective dose to maintain a normal neutrophil count should be established, administered SC. Initial dose adjustment to alternate day dosing with 30 MU (300 μg)/day is recommended. Further dose adjustment may be necessary. For titration, dose adjustments and dilution for infusion – see SmPC.

Contraindications: Hypersensitivity to filgrastim or any of the excipients of Accofil.

Warnings and Precautions: Traceability: In order to improve the traceability of granulocyte-colony stimulating factors (G-CSFs), the trade name of the administered product should be clearly recorded in the patient file. Not to be used to increase the dose of cytotoxic chemotherapy beyond established dose regimens. Not for use in patients with severe congenital neutropenia who develop leukaemia or have evidence of leukaemic evolution. Permanently discontinue in patients with clinically significant hypersensitivity. Do not administer to patients with a history of hypersensitivity to filgrastim or pegfilgrastim. Potential for immunogenicity. G-CSF can promote growth of myeloid cells in vitro and similar effects may be seen on some non-myeloid cells in vitro. Not indicated in patients with myelodysplastic syndrome or chronic myelogenous leukaemia. Particular care should be taken to distinguish the diagnosis of blast transformation of chronic myeloid leukaemia from acute myeloid leukaemia (AML). Caution in patients with secondary AML. Bone density monitoring may be indicated in patients with osteoporotic bone diseases treated with
Filgrastim for >6 months. Pulmonary adverse reactions, particularly interstitial pneumonia reported – discontinue and provide appropriate treatment if signs such as cough, fever, dyspnoea and pulmonary infiltrates develop. Capillary leak syndrome has been reported, patients should be monitored closely and receive standard symptomatic treatment. Glomerulonephritis has been reported, generally resolved after dose reduction or withdrawal of treatment. Urinalysis monitoring is recommended. Left upper abdominal and/ or shoulder tip pain should be evaluated for potential splenic enlargement or rupture. Some cases of fatal splenic rupture, spleen size should be carefully monitored. If patients with severe chronic neutropenia (SCN) develop abnormal cytogenetics, the risks and benefits of continuing filgrastim should be carefully weighed; filgrastim should be discontinued if MDS or leukaemia occur. ANC should be monitored closely, especially during the first few weeks of filgrastim therapy. A white blood cell count should be performed at regular intervals during filgrastim therapy. If leukocyte counts exceed 50 x 10^9/L after the expected nadir, discontinue filgrastim immediately. For PBPC mobilisation, discontinue or reduce dose if leukocyte counts rise to > 70 x 10^9/L. Platelet counts and haematocrit should be monitored closely for thrombocytopenia. Increased haematopoietic activity of the bone marrow in response to growth factor therapy has been associated with transient abnormal bone scans. Caution in sickle cell disease – crises (some fatal) reported. Do not use in patients with rare hereditary problems of fructose intolerance. Aortitis has been reported after granulocyte-colony stimulating factor (G-CSF) administration in healthy subjects and in cancer patients. Needle cover contains a derivative of latex. Accofil may have a minor influence on the ability to drive and use machines – see SmPC for further details of Warnings and Precautions.

**Pregnancy & Lactation:** Pregnancy: not recommended. Breast-feeding: risk to the breast-feeding child cannot be excluded.

**Adverse Events include:**

- **Adverse events which could be considered serious:** Very Common: Thrombocytopenia. Common: Sepsis, dyspnoea, severe splenomegaly, transfusion reaction, bronchitis, upper respiratory tract infection, urinary tract infection. Uncommon: Graft versus Host Disease, acute respiratory distress syndrome (may be fatal), respiratory failure (may be fatal), pulmonary oedema, interstitial lung disease, pulmonary haemorrhage, hypoxia, drug hypersensitivity, hypersensitivity, veno-occlusive disease. Rare: Severe splenic rupture (some cases fatal), exacerbation of rheumatoid arthritis, sickle cell anaemia with crisis, anaphylactic reaction, capillary leak syndrome, aortitis, Sweet’s syndrome (acute febrile neutrophilic dermatosis), glomerulonephritis. Frequency not known: Interstitial pneumonia, transformation to myelodysplastic syndrome or leukaemia in severe chronic neutropenia patients.

- **Other Very Common adverse events:** Anaemia, headache, diarrhoea, vomiting, nausea, alopecia, musculoskeletal pain, fatigue, mucosal inflammation, pyrexia, leukocytosis, leukapheresis.

- **Other Common adverse events:** Cutaneous vasculitis, haemoglobin decreased, decreased appetite, blood lactate dehydrogenase increased, dizziness, hypoaesthesia, paraesthesia, hypotension, hypertension, insomnia, haemoptysis, cough, oropharyngeal pain, epistaxis, constipation, oral pain, blood alkaline phosphatase increased, hepatomegaly, rash, erythema, muscle spasms, dysuria, haematuria, chest pain, asthenia, pain, malaise, oedema peripheral. Consult SmPC for details of other adverse events.

**Presentation and Price:** 30MU/0.5ml x 5 £284.20; 48MU/0.5ml x 5 £455.70

**Legal Category:** POM

**Further information is available from:** Accord-UK Ltd, Whiddon Valley, Barnstaple, Devon, EX32 8NS.

**Marketing Authorisation Numbers:** EU/1/14/946/001-018
Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.

Adverse events should also be reported to Accord-UK LTD on 01271 385257.