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Country	: Indonesia	Min. point size of text	: 7 pt
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Date	: 13-09-02021	Dimensions	: 355.9 x 215.6 mm
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Prepared by	: Azka Afina		

Printing Colour

Pantone Reflex Blue CVC

Technical Information

outline

Granocyte® 34
Lenograstim

Powder and solvent for solution for injection

SANOFI

IDENTIFICATION OF THE MEDICINAL PRODUCT

Name of Product

GRANOCYTE 34 (33.6 x 10^6 IU/ml) lyophilized powder in vial and solvent in prefilled syringe for injection or infusion (subcutaneous injection or intravenous infusion).

Qualitative and Quantitative composition

Lyophilisate :	per vial
Lenograstim* (INN) 33.6 x 10^6 IU**	263 micrograms
L-Arginine	10 mg
L-Phenylalanine	10 mg
L-Methonine	1 mg
Mannitol	25 mg
Polysorbate 20	0.1 mg
Hydrochloric acid	q.s pH 6.5
Solvent :	per pre-filled syringe
Water for injections	1 ml

* Recombinant glycoprotein (rHuG-CSF) equivalent to the human Granulocyte Colony Stimulating Factor isolated from CHU-2, a human cell line. Lenograstim is expressed and glycosylated in a mammalian host cell system, Chinese Hamster Ovary (CHO) cells.

** Measurement by the GNFS-60 *in vitro* bioassay in comparison with the WHO International Standard for human G-CFS.

Pharmaceutical form

Powder and solvent for solution for injection.

CLINICAL PARTICULARS

Therapeutic indications

- Reduction in the duration of neutropenia and associated complications in patients (with non-myeloid neoplasia) receiving an autologous or allogeneous bone marrow transplantation.
- Reduction in the duration of neutropenia and associated complications in patients during chemotherapy known to be associated with a significant incidence of febrile neutropenia.
- Mobilisation of Peripheral Blood Progenitor Cells (PBPCs).

Note: The safety of the use of GRANOCYTE 34 with anticancer agents characterized by cumulative myelotoxicity or predominant toxicity towards the platelet lineage (nitrosourea, mitomycin) has not been established. In these situations, the use of GRANOCYTE 34 might even increase the toxicities, particularly towards platelets.

Dosage and method of administration

Therapy should only be given in collaboration with an experienced oncology and/or haematology centre.
The recommended dose of GRANOCYTE 34 is 150 micrograms (19.2 x 10^6 IU) per m^2 and per day, a dose equivalent in efficacy to that of 5 micrograms (0.64 x 10^6 IU) per kg and per day:

- in chemotherapy-induced neutropenia for bone Marrow Transplantation (BMT),
- following established cytotoxic chemotherapy,
- in the mobilization of PBPCs after chemotherapy.

GRANOCYTE 34 is used in patients with a body surface area of up to 1.8 m^2.
In the mobilization of PBPCs when GRANOCYTE 34 is used alone, the recommended dose is 10 micrograms (1.28 x 10^6 IU) per kg and per day.

Adults:

After Bone Marrow Transplantation

GRANOCYTE 34 should be administered daily at the recommended dose of 150 micrograms (19.2 x 10^6 IU) per m^2 and per day by IV infusion lasting 30 minutes, diluted in isotonic saline serum or by subcutaneous injection starting the day following transplantation (see section "Instructions for use and handling"). Treatment should continue until the expected date of the nadir has passed and the neutrophil count has returned to a stable level compatible with treatment discontinuation, with a maximum of 28 days of treatment if necessary.
It is anticipated that by day 14 following bone marrow transplantation, 50% of patients will have recovered to a normal neutrophil count or to a count compatible with the discontinuation of the treatment.

After established cytotoxic chemotherapy

GRANOCYTE 34 should be administered daily at the recommended dose of 150 micrograms (19.2 x 10^6 IU) per m^2 and per day subcutaneous injection, starting the day following the end of chemotherapy (see section "instructions for use and handling"). Administration of GRANOCYTE 34 should continue until the expected date of the nadir has passed and the neutrophil count has returned to a stable level compatible with treatment discontinuation, with a maximum of 28 days of treatment if necessary.
A transient increase in neutrophil count can occur during the first two days of treatment, however the treatment must not be discontinuated, because with the continuation of treatment the nadir usually occurs earlier and recovery is quicker.
In PBPCs mobilization after chemotherapy, GRANOCYTE 34 should be administered daily at the recommended dose of 150 micrograms (19.2 x10^6 IU) per m^2 and per day by subcutaneous injection, starting the day after the end of chemotherapy until the expected date of the nadir has passed and the neutrophil count has returned to a stable level compatible with treatment discontinuation.
Leukapheresis should be performed when the post nadir leukocyte count is rising or after evaluation of $CD34^+$ cells count obtained by a validated method. In patients, who have not been intensively pretreated by chemotherapy, one leukapheresis is generally sufficient to obtain the minimum acceptable threshold of ≥ 2 x 10^6 $CD34^+$ cells collected per kg.
In order to mobilize PBPCs with GRANOCYTE 34 alone, it should be administered daily at the recommended dose of 10 micrograms (1.28 x 10^6 IU) per kg and per day by a subcutaneous injection for 4 to 6 days.
Leukapheresis should be performed between day 5 and 7.
In patients who have not been intensively pretreated by chemotherapy, one leukapheresis is generally sufficient to obtain the minimum acceptable threshold of ≥ 2 x 10^6 $CD34^+$ cells collected per kg.
In healthy donors, a 10 µg/kg daily dose administered subcutaneously for 5–6 days allows a $CD34^+$ cells collection ≥ 3 x 10^6/kg body weight with a single leukapheresis in 83% of subjects and with 2 leukapheresis in 97%.
Treatment must be administered only in cooperation with an establishment experienced in oncology and/or haematology.

Elderly:

Clinical trials with GRANOCYTE 34 included a small number of patients older than 70 but specific studies have not been performed in the elderly: therefore, specific dose recommendations cannot be made.

Children:

The safety and efficacy of GRANOCYTE 34 have been established in children older than 2 in bone marrow transplantation.

Contraindications

GRANOCYTE 34 is contraindicated in patients with known hypersensitivity to the product or to one of its constituents.
GRANOCYTE 34 should not be used to increase the dose intensity of myelotoxic chemotherapy beyond established doses and combinations since the drug could reduce myelotoxicity but has no effect on the general toxicity of chemotherapy.
GRANOCYTE 34 should not be administered concurrently with cytotoxic chemotherapy.
GRANOCYTE 34 should not be administered to patients:

- with myeloid neoplasia other than *de novo* acute myeloid leukemia.
- With *de novo* acute myeloid leukemia aged below 55 years, and/or
- With *de novo* acute myeloid leukemia with good cytogenetics, i.e. t(8; 21), t(15; 17) and inv (16).

Warnings and precautions for use

Malignant cell growth:

G-CSFs can promote growth of myeloid cells *in vitro* and similar effects may be observed in some non-myeloid cells *in vitro*.
The safety and efficacy of GRANOCYTE 34 in patients with myelodysplasia syndrome, secondary acute myeloid leukemia or chronic myelogenous leukemia have not been established. Therefore, GRANOCYTE 34 should not be used in these indications. Particular care should be taken to distinguish blast transformation of chronic myeloid leukemia from acute myeloid leukemia.
Clinical trials have not established whether GRANOCYTE 34 has an effect on the progression of myelodysplasic syndrome into acute myeloid leukemia.
Special caution is recommended when using GRANOCYTE 34 in any pre-leukemic syndrome situation.
As some non-specific tumors may exceptionally express a G-CSF receptor, special caution is recommended as unexpected tumor regrowth may occur during rHuG-CSF therapy.

Hyperleukocytosis:

During clinical trials, a leukocyte count more than 50 x 10^9/l has never been observed in any of the 174 patients treated with 5 micrograms per kg per day (0.64 x 10^6 IU/kg/day) following BMT. A white blood cells count greater than 70 x 10^9/l has been observed in less than 5% of patients who received chemotherapy and were treated with GRANOCYTE 34 at 5 micrograms per kg per day (0.64 million IU/ kg/day). No adverse events directly attributable to this degree of hyperleukocytosis have been reported. In view of the potential risks associated with severe hyperleukocytosis, a white blood cell count should be performed at regular intervals during GRANOCYTE 34 therapy.
If the leukocyte count exceeds 50 x 10^9/L after the expected date of the nadir, GRANOCYTE 34 should be discontinued immediately.

When GRANOCYTE 34 is used to mobilize PBPCs, suspension of treatment is recommended if leukocyte count exceeds 70 x 10^9/L.

Pulmonary adverse effects:

The onset of pulmonary signs, such as cough, fever and dyspnoea, in associated with radiological signs of pulmonary infiltrate and deterioration pulmonary function may be preliminary signs of adult respiratory distress syndroms (ARDS).
GRANOCYTE 34 should be discontinued and appropriate treatment should be given.

In Bone marrow transplantation

The effect of GRANOCYTE 34 on the incidence and severity of acute and chronic graft-versus-host disease has not been accurately determined.

Risks associated with intensification of chemotherapy doses:

The safety and efficacy of GRANOCYTE 34 remains to be established in the context of intensified chemotherapy.
GRANOCYTE 34 should not be used to reduce the intervals between chemotherapy courses beyond the established limits, nor to increase the established doses of chemotherapy. In a phase II chemotherapy intensification trial with GRANOCYTE 34, non-myeloid toxicities have become limiting factors.

Capillary leak syndrome

Capillary leak syndrome has been reported after G-CSF administration and is characterised by hypotension, hypoalbuminaemia, oedema and haemoconcentration. Lenograstim should be discontinued if patients develop symptoms of capillary leak syndrome and appropriate symptomatic treatment, which may include a need for intensive care, should be given (see section "Undesirable effects").

Glomerulonephritis

Glomerulonephritis has been reported in patients and donors receiving lenograstim. Generally, events of glomerulonephritis resolved after dose reduction or withdrawal of G-CSF. Urinalysis monitoring is recommended.

Aortitis has been reported after G-CSF administration in healthy subjects and in cancer patients. The symptoms experienced included fever, abdominal pain, malaise, back pain and increased inflammatory markers (e.g. C-reactive protein and white blood cell count). In most cases aortitis was diagnosed by CT scan and generally resolved after withdrawal of G-CSF.

Special precaution in PBPC mobilization:

Choice of mobilization method

Clinical trials carried out in the same patient population have shown that PBPCs mobilization was higher when GRANOCYTE 34 is used after chemotherapy than when used alone (measurements being made in the same laboratory). However, the choice between these two methods of mobilization should take into consideration the overall therapeutic objectives in each individual patient.

Previous exposure to cytotoxic agents and/or radiotherapy

In patients who have undergone previous intensive chemotherapy and/or radiotherapy, it may be difficult to obtain the minimum acceptable threshold of 2 X 10^6 $CD34^+$ cells per kg, and then a sufficient hematological recovery.
Transplantation of PBPCs should be planned early in the treatment course of patients and particular care paid to the number of PBPCs mobilized before administration of high-dose chemotherapy. If yields prove insufficient, transplant program must be replaced by other forms of treatment.

Determination of PBPC yields

Particular care should be paid to the method of quantification of PBPCs as the results of flow cytometric analysis of $CD34^+$ cell vary among laboratories. The recommendation of a minimum threshold of ≥ 2 x 10^6 $CD34^+$ cells per kg to obtain a correct haematological recovery is based upon results published in the literature. However, the minimum threshold is not clearly defined. Yields higher than 2 x 10^6 $CD34^+$ cells per kg are associated with faster recovery, including platelets, while lower yields are associated with slower recovery.

In Healthy Donors

The PBPC mobilization which is a procedure without direct benefit for healthy donors should be considered imperatively in accordance with local regulations as a for a bone marrow donation when they are established.
The efficacy and safety of GRANOCYTE 34 has not been assessed in donors aged over 60 years.
Therefore the procedure cannot be recommended in these patients. Based on some local regulation and lack of studies, minors donors should not be considered.
PBPC mobilization should be considered for donors who fit usual clinical and laboratory eligibility criteria for bone marrow donation.
Marked leukocytosis (WBC ≥ 50 x 10^9/L) was observed in 24% of subjects studied.
Thrombocytopenia (platelets < 100 x 10^9/L) , aphaeresis-related, was observed in 42% of subjects studies and values < 50x10^9/L were occasionally noted following leukapheresis without related clinical adverse events and with normal value-back in every cases.
In any case mobilization of peripheral blood progenitor cells should not be performed in donors who are treated with anticoagulants or who have shown defects in haemotasis. If more than one leukapheresis is required, particular attention should be paid to donors with a platelets < 100 x 10^9/L prior to aphaeresis : in general aphaeresis should not be performed if platelets < 75 x 10^9/L.
Insertion of a central venous catheter should be avoided if possible with consideration given to venous access in selection of donors. Data on long term follow-up of donors are available on a small number of subjects.
Transient cytogenetic changes have been observed in healthy donors following use of G-CSF. The implications of these changes are not known.
Up to 6 years, no emerging long term adverse events have been reported after donation of PBPC. Nevertheless a risk of promotion of a malignant myeloid clone is possible. Therefore, it is recommended that systematic record and tracking of same of the stem cell gift be made by the aphaeresis centers.

In allogenic peripheral stem cells recipients obtained after mobilization by GRANOCYTE 34

Allogenic stem cell grafting may be associated with an increased risk for chronic Graft Versus Host Disease (GVH), and long term data of graft functioning are sparse.

Other precautions

The safety and efficacy of GRANOCYTE 34 have not been established in patients with impaired renal or liver function.
In patients with decreased bone marrow reserves, for example due to prior intensive chemotherapy/ radiotherapy, neutrophil response is sometimes decreased and the safety of GRANOCYTE 34 has not been established.

Interactions with other medicines and other forms of interaction

Use of GRANOCYTE 34 is not recommended during the 24-hours period preceding or following chemotherapy, because of the sensitivity of rapidly dividing myeloid cells to cytotoxic chemotherapy.
Possible interactions with other growth factors of cytokines remain to be determined by clinical trials.

Pregnancy and lactation

The safety of GRANOCYTE 34 has not been established in pregnant women.
Animal studies in the rat and rabbit have failed to show any evidence of a teratogenic effect of GRANOCYTE 34. An increased spontaneous abortion rate was seen in the rabbit, but no malformations were found.
During pregnancy, the potential risk of GRANOCYTE 34 to the fetus must be weighed against the expected therapeutic benefit.
In the absence of data concerning penetration in the breast milk, treatment with GRANOCYTE 34 is not recommended during lactation.

Effects on the ability to drive or operate machines

None.

Undesirable effects

In Bone Marrow Transplantation

Particular attention must be paid to platelet recovery, since in controlled trials, the mean platelet count was lower in patients treated with GRANOCYTE 34 than in those who were given a placebo. However this did not lead to increased bleeding events and the median number of days between the transplantation and the last platelet transfusion was similar in both groups.
In controlled trials, the incidence of adverse events most frequently reported (15% in at least one of the treated groups) was identical in patients treated with GRANOCYTE 34 or placebo.
These adverse events were those usually observed in conditioning protocols and were apparently not attributable to GRANOCYTE 34. The events consisted of: stomatitis, fever, diarrhea, rash, abdominal pain, vomiting, alopecia, septic episod and infection.

In chemotherapy-induced neutropenia

The safety of GRANOCYTE 34 combined with cytotoxic agents with cumulative bone marrow toxicity or predominant toxicity vis-a-vis the platelet lineage (nitrosourea, mitomycin) has not been confirmed. The use of GRANOCYTE 34 might even lead to increased platelet toxicity in such circumstances.
In trials, the incidence of adverse events reported was the same in patients treated with GRANOCYTE 34 or placebo.
Effects most frequently reported were similar to those seen in patients treated with chemotherapy: alopecia, nausea, vomiting, fever and headache.
Bone pain and reactions at the injection site have been reported with a slightly higher incidence (about 10% and 5% respectively) in patients treated with GRANOCYTE 34.

PBPC mobilization in the peripheral blood

When GRANOCYTE 34 is administered to healthy subjects, the most commonly reported clinical adverse events were headache in 30%, bone pain in 23%, back pain in 17.5%, asthenia in 11%, abdominal pain in 6% and pain in 6% of subjects.
The risk of occurrence of pain is increased in subjects with high peak white blood cells values, especially when white blood cells ≥ 50 x 10^9/L.
Marked leukocytosis ≥ 50 x 10^9/L was reported in 24% of donors and thrombocytopenia (platelets < 100 x 10^9/L) aphaeresis-related in 42%.
Transient increase of ASAT and/or ALAT was observed in 12% of subjects and transient increase of alkaline phosphatase in 16%.

Disetujui oleh BPOM : 20 Desember 2021

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Prepared by	: Azka Afina		

Printing Colour

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Technical Information

outline

Other undesirable effects
Pulmonary infiltrates have been reported, in some cases with an outcome respiratory failure or adult respiratory distress syndrome (ARDS) which may be fatal.
In very rare cases, allergic reactions including isolated cases of anaphylactic shock have been reported during the course of GRANOCYTE 34 treatment.
Very rare cases of cutaneous vasculitis have been reported in patients treated with GRANOCYTE 34.
Very rare cases of Sweet's syndrome (acute febrile dermatosis), erythema nodosum and pyoderma gangrenosum have been reported. They were mainly described in patients with haematological malignancies, a condition known to be associated with neutrophilic dermatosis, but also in nonmalignant related neutropenia.
Very rare cases of Lyell syndrome have also been reported.
Increase of ASAT, ALAT and/or alkaline phosphatase has been reported during lenograstim treatment. In most cases, liver function abnormalities improved after treatment discontinuation.

Vascular disorders
Uncommon: Capillary leak syndrome
Rare frequency : Aortitis

Renal and urinary disorders:
Not known : Glomerulonephritis

Musculoskeletal, and connective tissue disorders
Very common : Musculoskeletal pain*
* Includes bone pain, back pain, arthralgia, myalgia and pain in extremity

Overdosage
In the animal, acute (up to 1000 micrograms per kg per day in the mouse) and subacute (up to 100 micrograms per kg per day in the monkey) toxicity studies have shown that the effects of overdosage were limited to reversible exacerbation of pharmacological effects.
The effects of GRANOCYTE 34 overdosage have not been established.
The discontinuation of GRANOCYTE 34 is usually accompanied by a 50% fall in circulating neutrophils within 1 to 2 days, with a return to normal levels in 1 to 7 days. A white blood cell count of approximately 50 x 10^9/L was seen in one of the three patients having received the highest doses of GRANOCYTE 34, of 40 micrograms per kg per day (5.12 x 106 IU per kg per day) on the 5th day of treatment.
In humans, doses of up to 40 micrograms per kg per day were not associated with toxic effects, with the exception of bone and muscle pains.

Pharmacological properties

Pharmacodynamic properties
CYTOKINE: granulocyte stimulation factor. LO3AA10.
GRANOCYTE 34 (rHuG-CSF) belongs to the cytokines group, biologically active protein which regulate cell differentiation and growth.
rHuG-CSF is a factor which stimulates the neutrophil progenitor cells, as shown by the CFU-S and CFU-GM cell count increases in peripheral blood.
GRANOCYTE 34 induces a notable increase in peripheral blood neutrophil count during the 24 hours following administration. This increase in neutrophils is dose-dependent between the range of 1 to 10 micrograms per kg per day. At the recommended dose, repeated administrations lead to an increase in neutrophil response. Neutrophils produced in response to GRANOCYTE 34 show normal chemotaxis and phagocytosis functions.
As with other haematopoietic growth factors, G-CSF has shown *in vitro* stimulating properties on human endothelial cells.
Use of GRANOCYTE 34 in patients who underwent Bone Marrow Transplantation or who are treated with cytotoxic chemotherapy leads to significant reductions in duration of neutropenia and its associated complications.
Administration of GRANOCYTE 34 either alone or after chemotherapy mobilizes haematopoietic progenitor cells (PBPCs) into the peripheral blood. These PBPCs can be harvested and infused after high dose chemotherapy, either in place of, or in combination to bone marrow transplantation. Reinfused PBPCs obtained by mobilization with GRANOCYTE 34 have proved to be able to reconstitute the haematopoiesis and accelerate the engraftment.
Independence of patients from platelet transfusion is hence achieved more rapidly in comparison with an autologous bone marrow transplant.
A pooled analysis of data from 3 double-blind placebo-controlled studies conducted in 861 patients (n = 411 ≥ 55 years) demonstrated a favorable benefit/risk ratio of lenograstim administration in patients over 55 years of age undergoing conventional chemotherapy for *de novo* acute myeloid leukemia, in the exception of AML with good cytogenetics, i.e. t(8; 21), t(15; 17) and inv (16).
In the subgroup of patients over 55 years, the benefit of the administration GRANOCYTE 34 appeared in terms of acceleration of neutrophil recovery, increase in the percentage of patients without infectious episode, and reduction in infection duration, reduction in the duration of hospitalization, reduction in the duration of I.V. antibiotherapy. However, these beneficial results were not associated with decreased severe or life-threatening infections incidence, nor with decreased infection related mortality.
Data from a double-blind placebo-controlled study, conducted in 446 patients with *de novo* AML showed that:
- In the 99 patients subgroup with good cytogenetics, the event-free survival was significantly lower in the lenograstim arm than in the placebo arm, and there was a trend towards a lower overall survival in the lenograstim arm than in the placebo arm.
- Those results concerning survival are not found again in subgroup of patients with not good cytogenetics.

Pharmacokinetic properties
Pharmacokinetic of GRANOCYTE 34 are dose and time dependent.
Following repeated administration, peak serum concentration at the end of IV infusion or after SC injection is proportional to the injected dose, without any evidence of a cumulative effect.
- At the recommended dose, the absolute bioavailability of GRANOCYTE 34 is 30%. Apparent volume of distribution (Vdss) is approximately 1L/kg and the mean residence time close to 7 hours following subcutaneous administrations.
- The apparent serum half-life after subcutaneous injection is approximately 3–4 hours at steady state (repeated administrations) and shorter (1–1.5 hours) after repeated IV infusion.
- Plasma clearance of rHuG-CFS increased 3-fold (from 50 up to 150 mL/min) following repeated subcutaneous administrations.
- A very small proportion of GRANOCYTE 34 is eliminated in unchanged form in urine (less than 1% of the dose) since it must be metabolized to endogenous peptides. The peak is close to 100 pg/mL/kg at the recommended dose by repeated subcutaneous injections. A positive correlation exists between dose and serum concentration and between neutrophil response and the total amount of GRANOCYTE 34 found in the serum.

Pharmaceutical particulars

Incompatibilities
Dilution of GRANOCYTE 34 (33.6 x 10^6 IU/vial) to a final concentration of less than 0.32 x 10^4 IU/ml (2.5 µg/ml) is not recommended.

Expiry date
Respect the date indicated on the outer packaging.

Shelf life:
30 months

Special precautions for storage
Do not store above 30°C. Do not freeze. The reconstituted solution of GRANOCYTE 34 must be administered within 24 hours after its preparation. Unused reconstituted or diluted solution should be discarded.

Nature and contents of containers
263 µg of lyophilisate in vial (glass) + 1 ml of solvent in pre-filled syringe (glass) + 2 needles (one 19 G for reconstitution and 26 G for administration).
One pack of 1 vial of lyophilized powder + 1 pre-filled syringe of solvent.
Reg. No.: DKI0185600344A1

Desciption
White lyophilised powder or mass

Instruction for use and handling
GRANOCYTE 34 vials are for single-dose use only.
The active substance and its solvent are overfilled by 5%. Hence the extractable volume of solvent is 1.05 ml used to reconstitute the lyophilisate with the aim of finally obtaining 1 ml of reconstituted solution of GRANOCYTE 34
Under aseptic conditions add the extractable content of a syringe pre-filled with 1.05 ml of solvent (water for injections) to the GRANOCYTE 34 vial (see here under diagrams).
For intravenous infusion, GRANOCYTE 34 must be diluted in 0.9% NaCl solution or in 5% dextrose solution.
Dilution of GRANOCYTE 34 to a final concentration of less than 0.32 x 106 IU/ml (2.5 µg/ml) is not recommended.
In any event, one vial of reconstituted GRANOCYTE 34 should be diluted in no more than 100 ml.
GRANOCYTE 34 is compatible with standard infusion devices (polyvinyl chloride bags and glass bottles) where diluted in 0.9% NaCl solution or in glass bottles where diluted in 5% dextrose solution.

HARUS DENGAN RESEP DOKTER

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

Manufactured by:
Sanofi Winthrop Industrie, Maisons-Alfort, France

Registered by:
PT Aventis Pharma, Jakarta – Indonesia

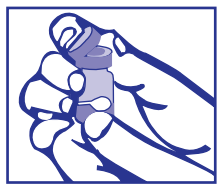
Diagram 1
Remove the plastic cap from the vial

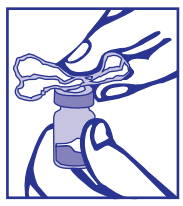
Diagram 2
Clean the rubber stopper.

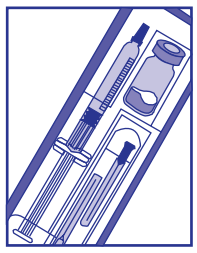
Diagram 3
Remove one pre-filled syringe from the blister and 2 needles [(one with the beige cone (19 G) and one with the brown cone (26 G)]

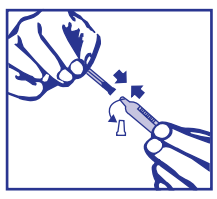
Diagram 4
Remove the tip-cap of the syringe and attach the beige cone needle to the syringe.

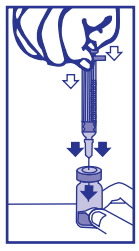
Diagram 5
Keeping the vial on a flat surface, push the needle through the rubber stopper and push the plunger rod to inject the solvent into the vial.

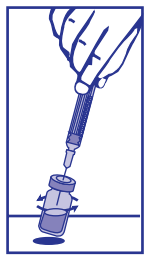
Diagram 6
Shake gently until it is completely dissolved (about 5 seconds). Do not shake vigorously.

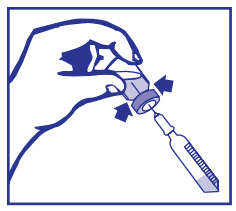
Diagram 7
Keeping the needle and the syringe attached to the vial, turn the vial upside down. Make sure the needle tip is in the solution.

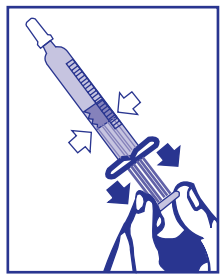
Diagram 8
Pull back slowly the plunger rod and withdraw the prescribed dose. Withdraw the required volume from the vial.

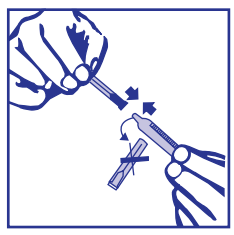
Diagram 9
Remove the beige cone needle from the syringe and replace it with the brown cone needle.

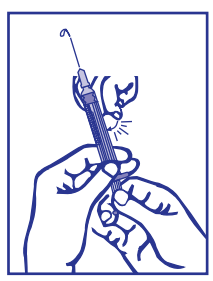
Diagram 10
Remove any air bubbles by gently tapping on the body of the syringe and push slowly the plunger rod to eliminate the air.


Diagram 11
If necessary, adjust the volume to be administered, GRANOCYTE 34 is now ready for injection. Administer immediately by subcutaneous injection.

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552074 - PI Granocyte

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Artwork by	: RPU	Revised by	: Azka Afina

Printing Colour

Pantone Reflex Blue CVC

Technical Information

outline

LEAFLET KEMASAN: INFORMASI BAGI PENGGUNA

Granocyte® 34
Lenograstim

SANOFI

Baca semua isi leaflet ini dengan seksama sebelum Anda mulai obat ini karena leaflet ini mengandung informasi penting untuk Anda.
- Simpan leaflet ini. Anda mungkin perlu membacanya lagi
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan kepada dokter atau apoteker Anda
- Obat ini hanya diresepkan untuk Anda. Jangan berikan ini kepada orang lain. Ini dapat membahayakan mereka, bahkan jika tanda-tanda penyakit mereka sama dengan Anda
- Jika Anda mengalami efek samping, bicarakan dengan dokter atau apoteker Anda. Ini termasuk kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Lihat bagian indikasi terapeutik, dosis dan cara pemberian, kontraindikasi, peringatan dan perhatian, interaksi dengan obat-obatan lain dan bentuk interaksi lainnya, kehamilan dan menyusui, efek dalam mengemudi atau menggunakan mesin, efek samping, dan overdosis.

Apa yang ada di leaflet ini:

1. Apa itu Granocyte 34 dan Granocyte 34 digunakan untuk apa
Nama obat Anda adalah Granocyte 34, serbuk dan pelarut untuk injeksi / larutan infus untuk injeksi (dalam leaflet ini disebut Granocyte 34). Granocyte 34 mengandung obat yang disebut lenograstim. Lenograstim merupakan sekelompok obat yang disebut sitokin.

Granocyte 34 bekerja dengan membantu tubuh Anda membuat lebih banyak sel darah yang melawan infeksi.
- Sel-sel darah ini dibuat di sumsum tulang Anda.
- Granocyte 34 mendorong sumsum tulang Anda untuk membuat lebih banyak sel yang disebut 'sel punca darah'.
- Ini kemudian membantu mengubah sel darah muda ini menjadi sel darah yang berfungsi penuh.
- Secara khusus, ini membantu menghasilkan lebih banyak sel darah putih yang disebut neutrofil. Neutrofil penting dalam melawan infeksi.

Granocyte 34 digunakan:

- **Setelah pengobatan kanker, jika tingkat sel darah putih Anda terlalu rendah (disebut 'neutropenia')**
  Beberapa perawatan untuk kanker (disebut juga 'kemoterapi') mempengaruhi sumsum tulang. Ini dapat menurunkan jumlah sel darah putih Anda. Hal ini mempengaruhi terutama pada neutrofil dan disebut sebagai 'neutropenia'. Hal ini berlangsung sampai tubuh Anda mampu menghasilkan lebih banyak sel darah putih. Ketika Anda memiliki jumlah neutrofil yang rendah, Anda lebih mudah untuk mendapatkan infeksi. Hal ini terkadang dapat sangat serius. Granocyte 34 akan membantu mengurangi waktu Anda memiliki tingkat sel yang rendah. Ini dilakukan dengan mendorong tubuh Anda untuk membuat sel darah putih baru.
- **Ketika Anda perlu meningkatkan sel induk darah Anda sendiri (disebut 'mobilisasi')**
  Granocyte 34 dapat digunakan untuk mendorong sumsum tulang Anda untuk menghasilkan sel induk darah. Ini disebut 'mobilisasi'. Ini bisa terjadi sendiri atau mungkin setelah kemoterapi. Sel-sel induk darah ini diambil dari darah Anda dan dikumpulkan menggunakan mesin khusus. Sel-sel induk darah kemudian dapat disimpan dan diberikan kembali kepada Anda melalui transfusi.
- **Setelah transplantasi sumsum tulang atau sel induk darah**
  Ketika Anda akan mendapatkan transplantasi sumsum tulang atau sel induk darah, Anda pertama kali diberikan kemoterapi dosis tinggi atau total iradiasi tubuh. Ini untuk membunuh sel yang sakit. Transplantasi sumsum tulang atau sel induk darah kemudian diberikan kepada Anda sebagai transfusi darah. Diperlukan waktu untuk sumsum tulang baru Anda untuk mulai memproduksi sel darah baru (termasuk sel darah putih). Granocyte 34 akan membantu tubuh Anda mempercepat pemulihan sel darah putih baru Anda.

Granocyte 34 dapat digunakan pada orang dewasa, remaja, dan anak-anak yang lebih dari 2 tahun.

2. Apa yang Perlu Anda Ketahui Sebelum Menggunakan Granocyte 34

Jangan menggunakan Granocyte 34:
- jika Anda alergi terhadap lenograstim atau salah satu bahan lain dari obat ini (tercantum dalam bagian komposisi). Tanda-tanda reaksi alergi termasuk: ruam, masalah menelan atau bernafas, pembengkakan bibir, wajah, tenggorokan atau lidah
- jika Anda mengidap sesuatu yang disebut 'phenylketonuria'
- jika Anda memiliki jenis kanker yang disebut 'kanker myeloid'. Namun, Anda dapat mengkonsumsi Granocyte 34 jika Anda baru saja didiagnosis 'leukemia myeloid akut' dalam kasus-kasus tertentu, jika Anda berusia lebih dari 55 tahun.
- jika Anda menjalani kemoterapi kanker pada hari yang sama.

Jangan gunakan obat ini jika salah satu hal di atas berlaku untuk Anda. Jika Anda tidak yakin, bicarakan dengan dokter atau apoteker Anda sebelum diberikan Granocyte 34.

Peringatan dan perhatian
Bicaralah dengan dokter atau apoteker Anda sebelum menggunakan obat ini:
- jika Anda pernah memiliki penyakit apa pun, terutama alergi, infeksi, masalah ginjal atau hati.
- jika Anda memiliki penyakit sel sabit atau sifat sel sabit karena Granocyte 34 berpotensi menyebabkan krisis sel sabit.

Harap beri tahu dokter Anda segera selama perawatan Granocyte 34, jika Anda:
- Mengalami bengkak di wajah atau pergelangan kaki Anda, darah dalam urin Anda atau urin berwarna coklat atau Anda merasa buang air kecil lebih sedikit dari biasanya

Jika Anda tidak yakin apakah ini berlaku untuk Anda, bicarakan dengan dokter atau apoteker Anda sebelum mengkonsumsi Granocyte 34.

Peradangan aorta (pembuluh darah besar yang mengangkut darah dari jantung ke tubuh) jarang dilaporkan pada pasien kanker dan donor sehat. Gejala-gejalanya dapat mencakup demam, sakit perut, malaise, nyeri punggung, dan penanda inflamasi yang meningkat. Beri tahu dokter Anda jika Anda mengalami gejala-gejala ini.

Anak-anak dan remaja
Bicaralah dengan dokter Anda sebelum minum obat ini:
- jika Anda atau anak Anda memiliki jenis kanker yang disebut "leukemia limfositik akut" dan jika Anda atau anak Anda berusia kurang dari 18 tahun

Obat-obatan lain dan Granocyte 34
Beri tahu dokter atau apoteker Anda jika Anda sedang atau baru saja mengkonsumsi obat lain. Ini termasuk obat-obatan yang diperoleh tanpa resep, termasuk obat-obatan herbal.

Jika Anda ingin menyumbangkan sel punca darah Anda dan Anda menjalani perawatan anti-koagulan (seperti warfarin atau heparin), pastikan dokter mengetahui hal ini sebelum Anda mulai mengkonsumsi Granocyte 34. Juga beri tahu mereka jika Anda tahu Anda memiliki masalah pembekuan darah lainnya.
Jika Anda diberikan kemoterapi anti kanker, jangan gunakan Granocyte 34 selama 24 jam sebelum terapi dimulai hingga 24 jam setelah terapi berakhir.

Kehamilan dan menyusui
Jangan gunakan obat ini jika Anda hamil, mungkin hamil atau menyusui, kecuali dokter Anda memberi tahu Anda bahwa itu perlu. Jika Anda sedang hamil atau menyusui, berpikir Anda mungkin sedang hamil atau berencana untuk memiliki bayi, mintalah saran dokter Anda sebelum mengkonsumsi obat ini. Granocyte 34 belum diuji pada wanita hamil atau menyusui.

Mengemudi dan menggunakan mesin
Efek Granocyte 34 pada kemampuan mengemudi atau menggunakan mesin atau alat tidak diketahui. Tunggu untuk melihat bagaimana Granocyte 34 mempengaruhi Anda sebelum mengemudi atau menggunakan alat atau mesin.

Granocyte 34 mengandung fenilalanin.
Fenilalanin mungkin berbahaya bagi Anda jika Anda memiliki sesuatu yang disebut 'fenilketonuria'. Komposisi ujung dari jarum suntik yang diisi sebelumnya mengandung karet lateks yang dapat menyebabkan reaksi alergi parah pada subjek yang memiliki kecenderungan.
(Lihat bagian jangan menggunakan Granocyte 34 di atas).

3. Cara menggunakan Granocyte 34
Granocyte 34 harus diberikan di bawah pengawasan pusat Onkologi atau Hematologi yang berpengalaman. Biasanya akan diberikan oleh dokter, perawat atau apoteker. Itu diberikan dalam injeksi atau infus.
Namun, beberapa pasien telah diajarkan cara memberikan suntikan ke diri mereka sendiri. Jika Anda memiliki pertanyaan tentang bagaimana obat ini diberikan, bicarakan dengan dokter, perawat, atau apoteker Anda.

Berapa banyak Granocyte 34 yang diberikan
Jika Anda tidak yakin mengapa Anda diberikan Granocyte 34 atau memiliki pertanyaan tentang berapa banyak Granocyte 34 diberikan kepada Anda, bicarakan dengan dokter, perawat, atau apoteker Anda.

Setelah transplantasi sumsum tulang, kemoterapi atau untuk mobilisasi sel induk darah setelah kemoterapi
- Dokter Anda akan menentukan berapa banyak Granocyte 34 yang akan diberikan kepada Anda tergantung pada luas permukaan tubuh Anda. Ini dihasilkan dengan menggunakan berat dan tinggi badan Anda. Ini diukur dalam 'meter persegi', yang ditulis sebagai 'm²'
- Dosis Granocyte 34 yang biasa adalah 19,2 MIU (150 mikrogram) untuk setiap m² area permukaan tubuh setiap hari. Dosis pada anak-anak yang lebih tua dari 2 tahun dan remaja sama dengan pada orang dewasa.
- Jumlah hari Anda mendapatkan Granocyte 34 akan ditentukan oleh dokter Anda. Anda mungkin diberikan hingga 28 hari
- Ketika Granocyte 34 diberikan untuk mobilisasi sel induk darah setelah kemoterapi, dokter Anda akan memberi tahu Anda kapan pengumpulan sel induk darah Anda akan terjadi

Untuk mobilisasi sel induk darah hanya dengan Granocyte 34
- Dokter Anda akan menentukan berapa banyak yang diberikan kepada Anda, tergantung pada berat badan Anda.
- Dosis Granocyte 34 yang biasa adalah 1,28 MIU (10 mikrogram) untuk setiap kg berat badan setiap hari. Dosis pada anak-anak yang lebih tua dari 2 tahun dan remaja sama dengan pada orang dewasa.
- Anda akan diberikan Granocyte 34 sebagai suntikan di bawah kulit selama 4 hingga 6 hari
- Pengumpulan sel induk darah Anda akan terjadi antara 5 dan 7 hari kemudian.

GRANOCYTE 34 juta IU / mL dapat digunakan pada pasien dengan luas permukaan tubuh hingga 1,8 m².

Jika Anda menggunakan lebih banyak Granocyte 34 dari yang seharusnya
Jika Anda diberikan obat ini oleh dokter, perawat atau apoteker, kemungkinan mereka tidak akan memberikan Anda terlalu banyak obat. Mereka akan memantau perkembangan Anda dan memeriksa dosisnya. Selalu tanyakan jika Anda tidak yakin tentang dosis obat ini.
Jika Anda terlalu banyak menggunakan Granocyte 34, beri tahu dokter atau langsung pergi ke rumah sakit. Bawa serta paket obat ini. Ini agar dokter tahu apa yang telah Anda gunakan. Anda mungkin mendapatkan efek samping yang sangat buruk jika terlalu banyak menggunakannya. Masalah yang paling mungkin Anda rasakan adalah nyeri otot dan tulang.

Jika Anda lupa untuk menggunakan Granocyte 34
Jangan gunakan dosis ganda untuk menebus suntikan yang terlupakan. Selalu sampaikan pada dokter Anda yang akan memberi tahu Anda apa yang harus Anda lakukan.

Tes darah
Dokter perlu memantau Anda saat Anda menggunakan obat ini. Mereka perlu melakukan tes darah secara teratur. Ini akan memantau tingkat perubahan sel-sel darah Anda (neutrofil, sel darah putih lainnya, sel darah merah, trombosit).
Tes darah lainnya yang mungkin digunakan oleh dokter yang dapat menunjukkan perubahan saat Anda menggunakan Granocyte 34. Jika Anda menjalani tes darah, penting untuk memberi tahu dokter bahwa Anda sedang menggunakan Granocyte 34. Jumlah sel darah putih Anda mungkin meningkat, jumlah trombosit Anda mungkin menurun dan mungkin ada peningkatan kadar enzim. Perubahan ini biasanya membaik setelah Anda berhenti menggunakan Granocyte 34. Jika Anda menjalani tes darah, penting untuk memberi tahu dokter bahwa Anda menggunakan Granocyte 34.

Jika Anda memiliki pertanyaan lebih lanjut tentang penggunaan obat ini, tanyakan kepada dokter atau apoteker Anda.

4. Kemungkinan efek samping
Seperti semua obat, obat ini dapat menyebabkan efek samping, walaupun tidak semua orang mendapatkannya.
Untuk pasien kanker dan donor sehat:

Berhentilah menggunakan Granocyte 34 dan segera beri tahu dokter Anda jika:
- Nyeri di sisi kiri atas perut atau bahu kiri Anda. Ini bisa menjadi tanda peningkatan ukuran limpa Anda. Ini adalah efek samping umum yang disebut splenomegali tetapi efek samping yang sangat jarang dapat menyebabkan limpa membelah.
- Anda memiliki reaksi alergi yang sangat serius yang disebut 'syok anafilaksis'. Ini adalah reaksi yang tiba-tiba mengancam jiwa. Tanda-tandanya meliputi merasa lemah, sulit bernapas atau pembengkakan pada wajah. Ini adalah efek samping yang sangat langka.
- Anda memiliki masalah pernapasan. Tanda-tandanya termasuk batuk, demam, atau Anda mungkin sulit bernapas. Ini bisa menjadi tanda-tanda Sindrom Gangguan Pernafasan Akut yang merupakan efek samping yang sangat jarang.
- Anda memiliki salah satu atau kombinasi dari efek samping berikut: bengkak, yang mungkin berhubungan dengan buang air lebih jarang, kesulitan bernapas, pembengkakan perut dan perasaan kenyang, dan perasaan lelah yang umum. Gejala-gejala ini umumnya berkembang secara cepat. Ini bisa merupakan gejala dari kondisi yang tidak biasa (mempengaruhi 1 dari 100 orang) yang disebut "Capillary Leak Syndrome" yang menyebabkan darah bocor dari pembuluh darah kecil ke tubuh Anda dan membutuhkan perhatian medis segera.
- Anda mengalami cedera ginjal (glomerulonefritis). Cedera ginjal telah terlihat pada pasien yang menerima Granocyte 34. Hubungi dokter Anda segera jika Anda mengalami bengkak di wajah atau pergelangan kaki Anda, urin yang berdarah atau urin berwarna coklat atau perhatikan urin lebih sedikit dari biasanya

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Beri tahu dokter atau apoteker sesegera mungkin jika Anda mengalami efek samping berikut:
Efek samping yang sangat umum (mungkin dapat mempengaruhi 1 atau lebih dari 10 orang):
- Nyeri pada tulang, otot, persendian, punggung dan di kaki serta lengan, sakit kepala, demam, dan / atau merasa sakit (mual). Jika itu terjadi rasa sakit dapat dikontrol dengan obat penghilang rasa sakit yang normal.
- Perubahan sementara dalam tes darah termasuk yang berhubungan dengan fungsi hati Anda, yang biasanya tidak memerlukan tindakan pencegahan tambahan dan normal setelah obat dihentikan.
- Setelah donasi sel induk darah Anda mungkin merasa lelah. Itu karena menyatunya dengan sel darah merah Anda. Jumlah sel darah putih Anda mungkin menjadi tinggi dalam waktu singkat. Anda juga mungkin mengalami penurunan jumlah trombosit yang bisa membuat Anda mengalami pendarahan atau memar lebih mudah dari biasanya.

Efek samping yang umum (mungkin dapat mempengaruhi 1 dari 10 orang):
- Reaksi di tempat injeksi.
- Merasa sakit yang umun dan nyeri termasuk sakit perut

Efek samping yang tidak biasa (mungkin dapat mempengaruhi 1 dari 100 orang):
- Batuk darah (hemoptisis).

Jarang (mungkin dapat memengaruhi 1 dari 1.000 orang):
- Pendarahan dari paru-paru (pendarahan paru).
- Peradangan aorta (pembuluh darah besar yang mengangkut darah dari jantung ke tubuh), lihat bagian 2.

Efek samping yang sangat jarang (mungkin dapat mempengaruhi 1 dari 10.000 orang):
- Masalah kulit seperti warna kulit yang berubah keunguan , bagian atas lengan atau kaki Anda dan kadang-kadang wajah atau leher disertai demam (tanda-tanda 'sindrom Sweet'). Mungkin juga timbul benjolan merah disertai demam dan sakit kepala (tanda-tanda 'sindrom Lyell'). Juga, masalah kulit lainnya seperti memar merah pada kaki atau bisul pada tubuh Anda disertai demam dan nyeri sendi.
- Reaksi alergi. Tanda-tandanya termasuk ruam, masalah menelan dan bernafas, pembengkakan bibir, wajah, tenggorokan atau lidah.

Pelaporan efek samping
Jika Anda mendapat efek samping apapun, katakan pada dokter, apoteker, atau perawat Anda. Ini termasuk kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Anda juga dapat melaporkan efek samping secara langsung (lihat detail di bawah).

UK - Skema Kartu Kuning
Situs web: www.mhra.gov.uk/yellowcard.
Irlandia - HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Faks: +353 1 6762517. Situs web: www.hpra.ie; E-mail: medsafety@hpra.ie. Dengan melaporkan efek samping Anda dapat membantu memberikan informasi lebih lanjut tentang keamanan obat ini

5. Cara menyimpan Granocyte 34
Jauhkan obat ini dari pandangan dan jangkauan anak-anak.

Jangan menggunakan salah satu bagian serbuk Granocyte 34 dan pelarut untuk kit solusi setelah tanggal kedaluwarsa (EXP). Tanggal kedaluwarsa untuk serbuk Granocyte 34 terdapat pada kotak bagian luar dan pada label di setiap botol Granocyte 34. Tanggal kedaluwarsa untuk pelarut (air untuk injeksi) diberikan pada label masing-masing ampul air untuk injeksi, atau di kedua label *pre-filled syringe* dan pada kertas foil blister.

Tanggal kedaluwarsa mengacu pada hari terakhir bulan itu.

Jangan simpan di atas 30 ° C. Jangan diletakkan dalam *freezer.*

Dianjurkan untuk diencerkan atau dilarutkan. Jika perlu, Anda dapat menyimpan larutan yang telah dilarutkan atau diencerkan hingga 24 jam pada 2 ° C -8 ° C (dalam lemari pendingin).
Jangan membuang obat apa pun melalui wastafel atau pembuangan limbah rumah tangga. Tanyakan apoteker Anda bagaimana cara membuang obat yang tidak lagi Anda gunakan. Langkah-langkah ini akan membantu melindungi lingkungan.

6. Isi paket dan informasi lainnya

Apa kandungan Granocyte 34
- Zat aktifnya adalah lenograstim (rHuG-CSF) 33,6 juta Unit Internasional (setara dengan 263 mikrogram) per mL setelah diencerkan.
- Bahan lain dalam serbuk adalah arginin, fenilalanin, metionin, manitol (E421), polisorbat 20 dan asam hidroklorat encer.
  Eksipien yang diketahui memiliki aksi atau efek yang dikenali: fenilalanin
- Pelarut yang digunakan untuk melarutkan larutan adalah Air untuk Injeksi

Seperti apa bentuk Granocyte 34 dan isi dari paketnya
Granocyte 34 tersedia dalam bentuk [bubuk dan pelarut untuk larutan untuk injeksi / infus dalam *pre-filled syringe*].

Serbuk dalam botol + 1 mL pelarut dalam *pre-filled syringe* dengan dua jarum (jarum putih yang lebih besar untuk pengenceran (19G) dan yang lebih kecil berwarna cokelat untuk pemberian (26G))

Granocyte 34 tersedia dalam ukuran paket isi 1.

Deskripsi
Serbuk injeksi liofilisasi berwarna putih

Produsen
SANOFI WINTHROP INDUSTRIE, Usine de Maisons-Alfort, 180 rue Jean-Jaurès, BP40
94702 Maisons-Alfort - Cedex –France

Informasi berikut ditujukan hanya untuk profesional medis atau kesehatan

Informasi praktis tentang persiapan dan penanganan produk obat untuk profesional medis atau kesehatan
Vial Granocyte 34 hanya untuk penggunaan dosis tunggal.

Mengingat kemungkinan risiko kontaminasi mikroba, *pre-filled syringe* dan pelarutnya hanya untuk penggunaan tunggal.

Granocyte 34 digunakan melalui subkutan dan intravena.

Persiapan untuk melarutkan sediaan
Tambahkan secara aseptik isi dari satu *pre-filled syringe* vial Granocyte 34 menggunakan jarum 19G.
- Larutkan dengan perlahan sampai larut sepenuhnya.
- Jangan dikocok dengan keras
- Larutan yang dilarutkan nampak transparan dan bebas partikel.
- Tarik volume yang diperlukan dari larutan yang dilarutkan dari vial, menggunakan jarum 19G.
- Berikan segera dengan injeksi subkutan menggunakan jarum 26G.

Pada kasus penggunaan intravena, Granocyte 34 harus diencerkan setelah dilarutkan
Granocyte 34 kompatibel dengan cara penggunaan yang umum untuk diinjeksikan ketika diencerkan:
- dalam larutan salin 0.9% (kemasan polivinil klorida dan botol kaca)
- atau dalam larutan dekstrosa 5% (botol kaca)

Pengenceran GRANOCYTE 34 juta IU / mL ke konsentrasi akhir kurang dari 0,32 juta Unit Internasional / mL (2,5 µg / mL) tidak dianjurkan. 1 vial GRANOCYTE 34 juta IU / mL yang dilarutkan tidak boleh diencerkan dalam lebih dari 100 mL dalam keadaan apa pun.

Setiap produk / sisa bahan yang tidak digunakan harus dibuang sesuai dengan persyaratan setempat

INN: lenograstim

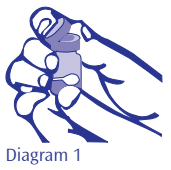


Diagram 1

Lepaskan tutup plastik dari vial

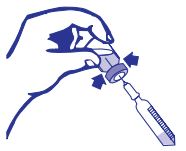


Diagram 7

Jaga agar jarum dan *syringe* menempel pada vial, balikkan vial. Pastikan ujung jarum masuk ke dalam larutan

Diagram 2

Bersihkan sumbatan karet

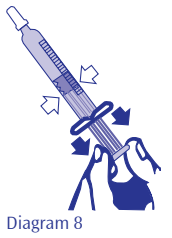


Diagram 8

Tarik kembali batang pendorong dan tarik sesuai dosis yang ditentukan. Tarik volume yang diperlukan dari vial.

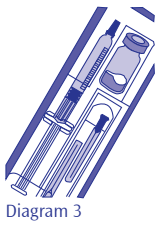


Diagram 3

Keluarkan satu *pre-filled syringe* dari blister dan dua jarum (satu dengan tutup berwarna krem (19G) dan satu dengan tutup berwarna coklat (26G)

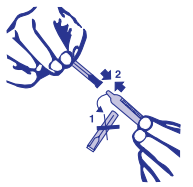


Diagram 9

Lepaskan tutup jarum berwarna krem dari *syringe* dan gantikan dengan tutup jarum berwarna coklat

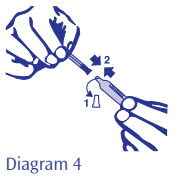


Diagram 4

Lepaskan *tip-cap* dari *syringe* dan pasang jarum dengan tutup berwarna krem ke *syringe*

Diagram 10

Hilangkan gelembung udara dengan cara mengetuk *body syringe* dengan perlahan dan dorong batang pendorong dengan perlahan untuk menghilangkan udara

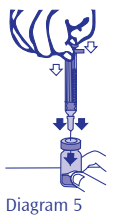


Diagram 5

Letakkan vial pada permukaan yang rata, suntikkan jarum ke dalam sumbatan karet dan dorong batang pendorong untuk menyuntikkan larutan ke dalam vial

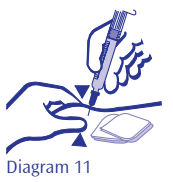


Diagram 11

Bila perlu, sesuaikan volume yang akan diberikan. Granocyte 34 sekarang siap untuk diadministrasikan. Berikan segera dengan injeksi subkutan

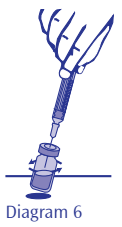
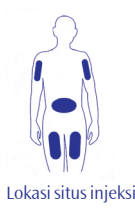


Diagram 6

Kocok dengan lembut sampai larut sempurna (sekitar 5 detik). Jangan dikocok dengan kuat



Lokasi situs injeksi untuk pemberian subkutan

HARUS DENGAN RESEP DOKTER

Pada proses pembuatannya bersinggungan dengan bahan bersumber babi

Diproduksi oleh:
Sanofi Winthrop Industrie, Maisons-Alfort, France

Diregistrasikan oleh:
PT Aventis Pharma, Jakarta – Indonesia

Reg. No.: DKI0185600344A1

Disetujui oleh BPOM : 20 Desember 2021

EREG10002212100561

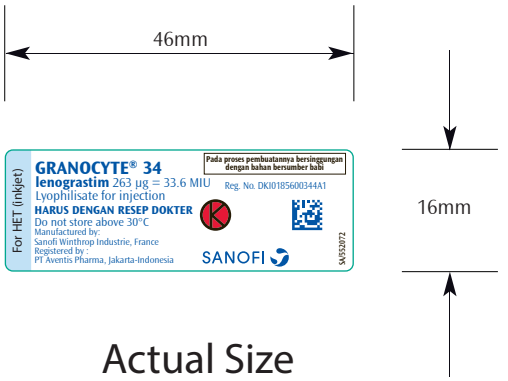
552075 - PIL Granocyte

Plant:	JAKARTA - INDONESIA
Packaging material code:	552075
Packaging material name:	PIL Granocyte
Second packaging material code:	
VISTAlink folder number:	4171514
VISTAlink PDF version:	4

This document has been digitally signed by the following people within the VISTAlink system, following the sanofi group guidelines.

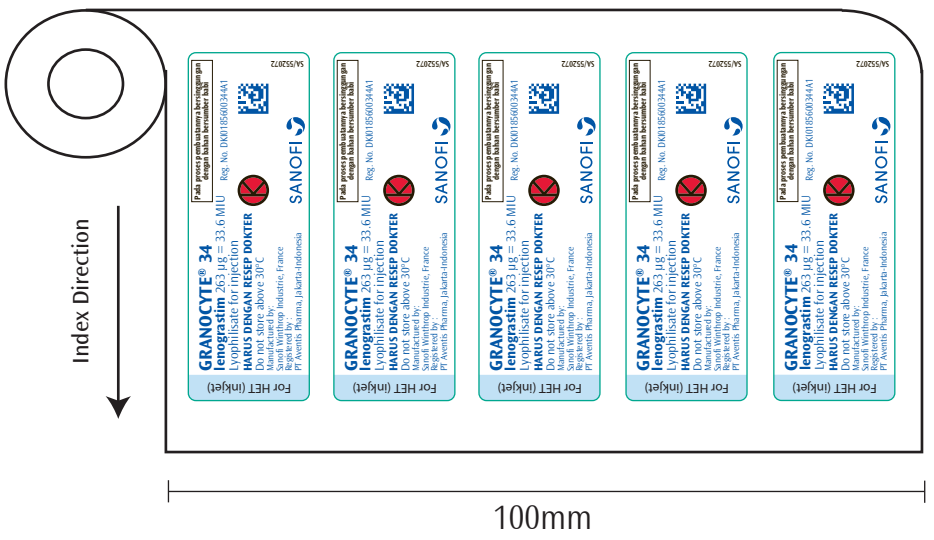
Reason	Signed by	Date
Market regulatory validation	Iin Ruslan (Indonesia Regulatory team)	13/10/2021 05:52:11
Plant quality validation	Melia Gunawan (Jakarta Quality Assurance team)	13/10/2021 05:55:27
Plant final technical validation	Lutfi AbdulKarim (Jakarta packaging team)	14/10/2021 10:29:33
Plant ready to print	Azka Afina (Jakarta Artwork team)	25/10/2021 08:59:52

Disetujui oleh BPOM : 20 Desember 2021 EREG10002212100561



Actual Size

Scale up 2x



Dalam Bentuk Roll Label

HET will be inkjet during redressing process in plant

SAP / ID. number : Label Granocyte / 552072

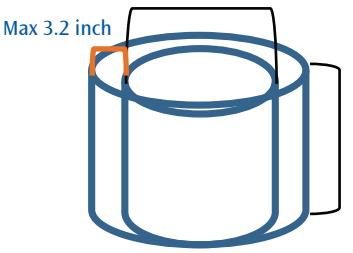
Film code : SA/552072

Country : Indonesia
Version number : 1
Date : 06-09-2021
Material : Chromcoated adhesive 85 g/m²
Data Matrix : 55207201
Prepared by : Azka Afina

Min. point size of text : 5 pt
Type of text : Ocean Sans Pro
Dimensions : 46 x 16 mm
Printing Colour : P. Reflex Blue CVC
: P. 186 CVC
: P. Black CVC

Technical Information

Ø Core 76.2 mm (3 inch)



Disetujui oleh BPOM : 20 Desember 2021

EREG10002212100561

552072 - Label Granocyte

Plant:	JAKARTA - INDONESIA
Packaging material code:	552072
Packaging material name:	Label Granocyte
Second packaging material code:	
VISTAlink folder number:	4171512
VISTAlink PDF version:	1

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Market regulatory validation	Iin Ruslan (Indonesia Regulatory team)	14/09/2021 12:06:42
Plant quality validation	Melia Gunawan (Jakarta Quality Assurance team)	16/09/2021 08:53:57
Plant final technical validation	Lutfi AbdulKarim (Jakarta packaging team)	16/09/2021 11:24:15
Plant ready to print	Azka Afina (Jakarta Artwork team)	23/09/2021 09:15:58

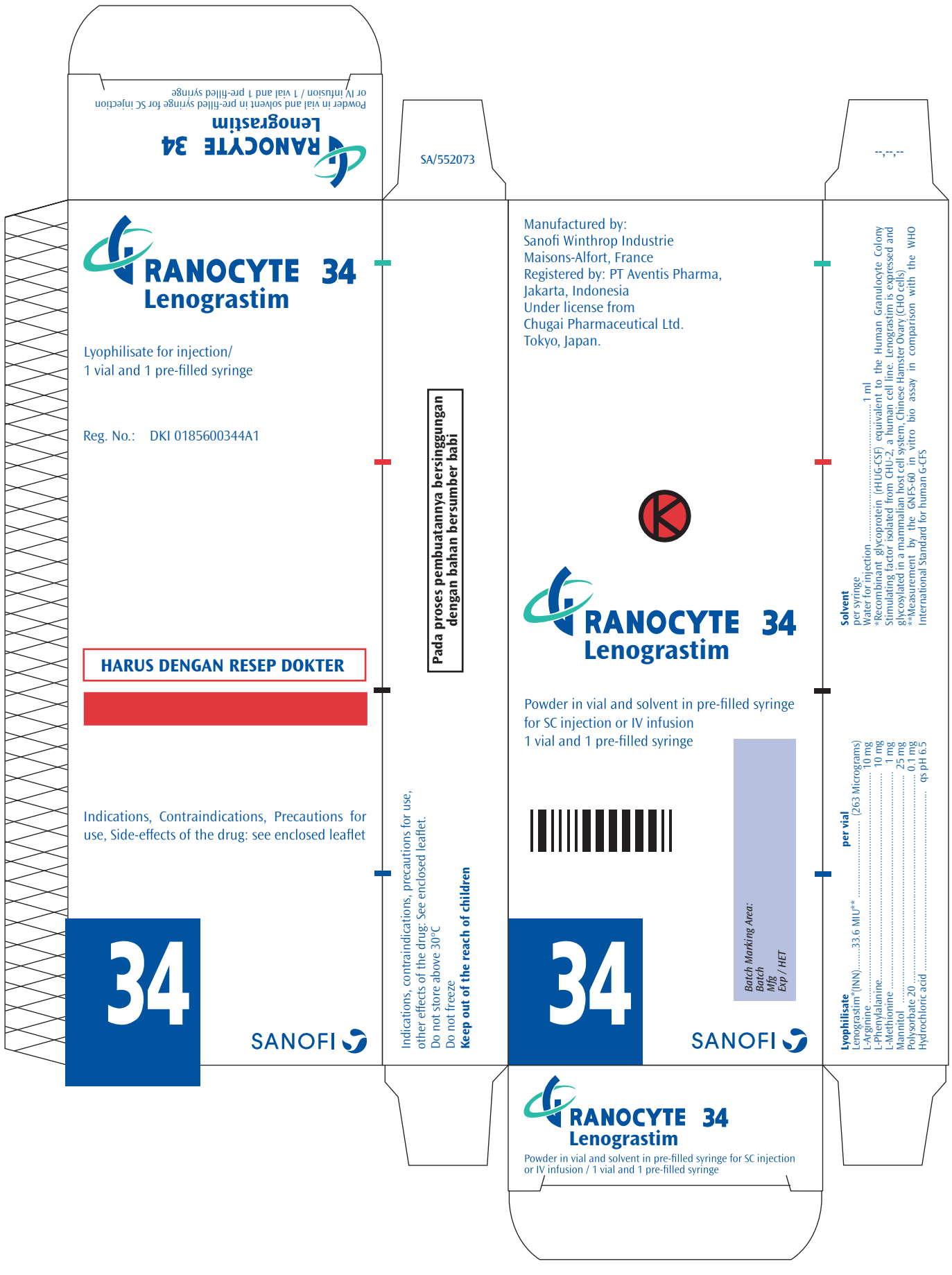
Disetujui oleh BPOM : 20 Desember 2021 EREG10002212100561

SAP / ID. number : Folding Box Granocyte / 552073		Film code : SA/552073	
Country	: Indonesia	Min. point size of text	: 6 pt
Version number	: 1	Type of text	: Ocean Sans Family
Date	: 29-07-2021	Dimensions	: 60 x 24 x 165 mm
Material	: Ivory Carton 300 g/m²	Printing Colour	
Pharmacode	: 20731	P. Reflex Blue	P. 186 CVC
Prepared by	: RPU	P. 3265 CVC	P. Black CVC
Revised by	: Azka Afina H.		

Technical Information

batchmarking area

Batch No, Mfg date, Exp date, HET *will not appear on the film. it will be printed using inkjet printer*



Disetujui oleh BPOM : 20 Desember 2021

EREG10002212100561

552073 - Folding Box Granocyte

Plant:	JAKARTA - INDONESIA
Packaging material code:	552073
Packaging material name:	Folding Box Granocyte
Second packaging material code:	
VISTAlink folder number:	4171511
VISTAlink PDF version:	1

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Reason	Signed by	Date
Market regulatory validation	Iin Ruslan (Indonesia Regulatory team)	14/09/2021 10:25:42
Plant quality validation	Melia Gunawan (Jakarta Quality Assurance team)	16/09/2021 08:49:51
Plant final technical validation	Lutfi AbdulKarim (Jakarta packaging team)	16/09/2021 11:22:09
Plant ready to print	Azka Afina (Jakarta Artwork team)	23/09/2021 09:15:09

Disetujui oleh BPOM : 20 Desember 2021 EREG10002212100561