Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Vinorelbine Ebewe 10mg/ml concentrate for solution for infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1ml concentrate for solution for infusion contains 10 mg Vinorelbine (as tartrate)
Each 5ml concentrate for solution for infusion contains 50 mg Vinorelbine (as tartrate)

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Concentrate for solution for infusion

Clear, colourless to pale yellow solution

The diluted solution for infusion is a clear, colourless or pale yellow solution

pH: 3.0-4.0

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Non-small cell lung cancer

Advanced breast cancer

4.2 Posology and method of administration

For intravenous infusion only
Vinorelbine® should be administered under the supervision of a physician with extensive experience in therapy with cytostatics.

Strictly intravenous administration after appropriate dilution.
Intrathecal administration of Vinorelbine® may be fatal.
Instructions for use and handling: refer to section 6.6.

Before application it is extremely important to ensure that the intravenous needle is positioned in the vein.

Leakage into surrounding tissue during administration of vinorelbine may cause considerable irritation. If extravasation occurs, the injection should be discontinued immediately, and any remaining portion of the dose should then be introduced into another vein.

It is recommended to infuse Vinorelbine® over 6-10 minutes after dilution in 20−50 ml of sodium chloride 9 mg/ml (0.9%) solution for injection or in glucose solution for injection 5%.
Administration should always be followed with at least 250 ml of an isotonic solution infusion to flush the vein.

Adults*:*

Non-small cell lung cancer

As monotherapy the usual dose is 25-30 mg/m^2, administered once weekly.
In combination therapy the same dose may be administered, but the number of applications are reduced so that 25-30 mg/m^2 is given e.g. day 1 and 5 every third week or day 1 and 8 every third week according to the regimen.

Metastatic breast cancer
The normal dose is 25-30mg/m^2, administered once weekly.

Maximum dosage:
The maximum tolerated dose per administration: 35.4mg/m^2 body surface area.

Administration in the elderly
Clinical experience has not identified relevant differences among elderly patients with regard to the response rate, although greater sensitivity in some of these patients cannot be excluded. Age does not modify the pharmacokinetics of vinorelbine.

Administration in patients with liver insufficiency
The pharmacokinetics of vinorelbine is not modified in patients presenting moderate or severe liver impairment. Nevertheless as a precautionary measure a reduced dose of 20mg/m^2 and close monitoring of haematological parameters is recommended in patient with severe liver impairment (refer to sections 4.4 and 5.2)

Administration in patients with renal insufficiency
Given the minor renal excretion, there is no pharmacokinetic justification for reducing the dose of vinorelbine in patients with renal insufficiency.
During therapy the hematologic condition of the patient should be carefully monitored.

Administration in children
Safety and efficacy in children have not been established and administration is therefore not recommended.

4.3 Contraindications

- Known hypersensitivity to Vinorelbine or other vinca alkaloids, or to any of the constituent.
- Neutrophil count <1500/m^3 or severe infection current or recent (within 2 weeks)
- Platelet count < 100000/mm^3
- Breastfeeding should be discontinued during treatment with Vinorelbine (refer to 4.6)
- In combination with yellow fever vaccine (refer to section 4.5)

4.4 Special warnings and precautions for use

Special warnings

Vinorelbine® should be administered under the supervision of a physician experienced in the use of chemotherapy. Vinorelbine concentrate for solution for infusion must only be administered by the intravenous route. The use of intrathecal route is contraindicated.
Since inhibition of the hematopoietic system is the main risk associated with Vinorelbine®, close haematological monitoring should be undertaken during treatment (determination of haemoglobin level and the leukocyte, neutrophil and platelet counts on the day of each new administration).

The dose limiting adverse reaction is mainly neutropenia. This effect is non-cumulative, having its nadir between 7 and 14 days after the administration and is rapidly reversible within 5 to 7 days. If the neutrophil count is below 1500/mm3and/or the platelet count is below 100000/mm3, then the treatment should be delayed until recovery.

If the patient presents signs or symptoms suggestive of infection, a prompt investigation should be carried out.

Interstitial lung disease has been reported more frequently in the Japanese population. Special attention should be

exercised for this specific population.

Special precautions for use

All contact with the eye should be strictly avoided: risk of severe irritation and even corneal ulceration if the drug is sprayed under pressure. Immediate liberal washing of the eye with normal saline solution should be undertaken if any contact occurs and contact an ophthalmologist.

Special care should be taken when prescribing for patients with history of ischemic heart disease (refer to section 4.8).

The pharmacokinetics of Vinorelbine ® is not modified in patients presenting moderate or severe liver impairment. For dosage adjustment in this specific patient group, refer to section 4.2.

As there is a low level of renal excretion there is no pharmacokinetic rationale for reducing the dose of Vinorelbine ® in patients with impaired kidney function.
Refer to section 4.2.

Vinorelbine ® should not be given concomitantly with radiotherapy if the treatment field includes the liver.

This product is specifically contra-indicated with yellow fever vaccine and its concomitant use with other live attenuated vaccines is not recommended.

To avoid the risk of bronchospasm – especially in combination therapy with mitomycin C appropriate prophylaxis may be considered. Outpatients should be informed that in case of dyspnoea a doctor has to be informed.
Caution must be exercised when combining vinorelbine and strong inhibitors or inducers of CYP3A4 (refer to Section 4.5 – Interactions specific to vinorelbine), and its combination with phenytoin (like all cytotoxics) and with itraconazole (like all vinca-alkaloids) is not recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Interactions common to all cytotoxics:
Due to the increase of thrombotic risk in case of tumoral diseases, the use of anticoagulative treatment is frequent. The high intra-individual variability of the coagulability during diseases, and the eventuality of interaction between oral anticoagulants and anticancer chemotherapy required, if it is decided to treat the patient with oral anticoagulants, to increase frequency of the INR (International Normalised Ratio) monitoring.

- Concomitant use contraindicated:

Yellow fever vaccine: risk of fatal generalised vaccine disease (refer to section 4.3).

- Concomitant use not recommended :

Live attenuated vaccines (for yellow fever vaccine, see concomitant use contraindicated): risk of generalised vaccine disease, possibly fatal. This risk is increased in patients already immunodepressed by their underlying disease. It is recommended to use an inactivated when exists (poliomyelitis) (refer to section 4.4).

Phenytoin: risk of exacerbation of convulsions resulting from the decrease of phenytoin digestive absorption by cytotoxic drug or loss of efficacy of the cytotoxic drug due to increased hepatic metabolism by phenytoin.

- Concomitant use to take into consideration:

Ciclosporine, tacrolimus: excessive immunodepression with risk of lymphoproliferation

Interactions specific to vinca-alkaloids:

- Concomitant use not recommended:

Itraconazole: increased neurotoxicity of vinca-alkaloids due to the decrease of their hepatic metabolism.

- Concomitant use to take into consideration:

Mitomycin C: risk of bronchospams and dyspnoea are increased, in rare case an interstitial pneumonitis was observed.
As vinca-alkaloids are known as substrates for P-glycoprotein and concurrent treatment with other drugs that inhibit (i.e. ritonavir, clarithromycin, cyclosporine, verapamil, quinidine) or induce (see list of CYP 3A4 inducers given below) the same transport protein can affect the concentration of Vinorelbine. In the absence of specific study, caution should be exercised when combining Vinorelbine with strong modulators of this membrane transporter

Interactions specific to Vinorelbine:

- The combination of vinorelbine with other drugs with known bone marrow toxicity is likely to exacerbate the myelosuppressive adverse effects.
  As CYP 3A4 is mainly involved in the metabolism of vinorelbine, combination with strong inhibitors of this isoenzyme (e.g. ketoconazole, itraconazole, HIV protease inhibitors, erythromycin, clarithromycin, telithromycin, neftazodone) could increase blood concentrations of vinorelbine and combination with strong inducers of this isoenzyme (e.g. rifampicin, phenytoin, phenobarbital, carbamazepine, Hypericum perforatum) could decrease blood concentrations of vinorelbine (see section 4.4).

- There is no mutual pharmacokinetic interaction when combining vinorelbine with cisplatin over several cycles of treatment. However, the incidence of granulocytopenia associated with vinorelbine use in combination with cisplatin is higher than associated with vinorelbine single agent.

- An increased incidence of grade 3/4 neutropenia has been suggested when intravenous vinorelbine and lapatinib were associated in one clinical phase I study. In this study, the recommended dose of intravenous form of vinorelbine in a 3-weekly schedule on day 1 and day 8 was 22.5 mg/m^2 when combined with daily lapatinib 1000 mg. This type of combination should be administered with caution.

4.6 Fertility, pregnancy and lactation

Pregnancy:
There are insufficient data available on the use of vinorelbine in pregnant women. Studies in animals have shown embryotoxicity and teratogenicity (see section 5.3). On the basis of the results of animal studies and the pharmacological action of the medicinal product, there is a potential risk of embryonic and foetal abnormalities.

Vinorelbine should therefore not be used during pregnancy, unless the individual awaited benefit clearly outweighs the potential risks. Vinorelabine may only be administered on strict indication, in which context the benefits of the drug for the mother must be weighed against the possible dangers to the foetus and be monitored carefully.

If pregnancy occurs during treatment, the patient should inform their doctor. The patient should be informed about the risks for the unborn child. The possibility of genetic counselling should be considered.

Women of child-bearing potential:
Women of child-bearing potential must use effective contraception during treatment with vinorelbine and up to 3 months after treatment finishes.

Lactation:
It is not known whether vinorelbine is excreted in human breast milk. The excretion of vinorelbine in milk has not been studied in animal studies. A risk to the suckling children cannot be excluded therefore breast feeding must be discontinued before starting treatment with vinorelbine (refer to section 4.3).

Fertility:

Men being treated with vinorelbine are advised not to father a child during and minimally up to 3 months after treatment. Prior to treatment, advice should be sought for conserving sperm due to the chance of irreversible infertility as a consequence of treatment with vinorelbine.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed but on the basis of the pharmacodynamics profile vinorelbine does not affect the ability to drive and use machines. However, caution is necessary in patient treated with vinorelbine considering some adverse effects of the drug.

4.8 Undesirable effects

Adverse reactions reported as more than isolated cases are listed below, by system organ class and by frequency. *Frequencies are defined as: very common (> 1/10), common (> 1/100, < 1/10), uncommon (> 1/1,000, < 1/100), rare (> 1/10,000, < 1/1,000), very rare (< 1/10,000),* according to the MedDRA frequency convention and system organ classification.

The most commonly reported adverse drug reactions are bone marrow depression with neutropenia, anaemia, neurologic disorders, gastrointestinal toxicity with nausea, vomiting, stomatitis and constipation, Transient elevations of liver function tests, alopecia and local phlebitis.

Additional adverse reactions from post marketing experience has been added according to the MedDRA classification with the frequency *Not known*

Detailed Adverse Reactions Information:

Reactions were described using the W.H.O classification (grade 1=G1 ; grade 2=G2 ; grade 3=G3 ; grade 4=G4 ; grade 1-4=G1-4) ; grade 1-2=G1-2 ; grade 3-4=G3-4).

Infections and infestations

Common: Infection bacterial, viral or fungal at different localization (respiratory, urinary, GI tract…) mild to moderate and usually reversible with an appropriate treatment.
Uncommon: Severe sepsis with other visceral failure.
Septicaemia
Very rare: Complicated septicaemia and sometimes fatal.
Not known: Neutropenic sepsis

Blood and lymphatic system disorders

Very common: Bone marrow depression resulting mainly in neutropenia (G3: 24.3%; G4: 27.8%), reversible within 5 to 7 days and non-cumulative over time.
Anaemia (G3-4: 7.4%),
Common: Thrombocytopenia (G3-4: 2.5%) may occur but are seldom severe
Not known: Febrile neutropenia
Pancytopenia

Immune system disorders

Not known: Systemic allergic reactions as anaphylaxis, anaphylactic shock or anaphylactoid type reaction

Endocrine disorders

Not known: Inappropriate antidiuretic hormone secretion (SIADH).

Metabolism and nutrition disorders

Rare: Severe hyponatraemia
Not known: Anorexia

Nervous system disorders
Very common: Neurologic disorders (G 3-4: 2.7%) including loss of deep tendon reflexes
Weakness of the lower extremities has been reported after a prolonged chemotherapy
Uncommon: Severe paresthesias with sensory and motor symptoms are infrequent.
Very rare: Guillain Barre Syndrome
These effects are generally reversible.

Cardiac disorders
Rare: Ischemic heart disease (angina pectoris, myocardial infarction, sometimes fatal)
Very rare: Tachycardia, palpitation and heart rhythm disorders.

Vascular disorders
Uncommon: Hypotension, hypertension, flushing and peripheral coldness
Rare: Severe hypotension, collapse

Respiratory system, thoracic and mediastinal disorders
Uncommon: Dyspnoea and bronchospasm may occur in association with Vinorelbine treatment as with other vinca alkaloids.
Rare: Interstitial pneumopathy (sometimes fatal) has been reported in particular patients treated with Vinorelbine in combination with mitomycin.

Gastrointestinal disorders
Very common: Stomatitis (G1-4: 15% with Vinorelbine as single agent)
Nausea and vomiting (G 1-2: 30.4% and G 3-4: 2.2%).
Anti-emetic therapy may reduce their occurrence. Constipation is the main symptom (G 3-4: 2.7%) which rarely progresses to paralytic ileus with Vinorelbine as single agent and (G3-4: 4.1%) with the combination of Vinorelbine and other chemotherapeutic agents.
Common: Diarrhoea usually mild to moderate and oesophagitis may occur.
Rare: Paralytic ileus, treatment may be resumed after recovery of normal bowel mobility.
Pancreatitis has been reported.

Hepatobiliary disorders
Very common: Transient elevations of liver function tests (G 1-2) without clinical symptoms were reported (SGOT in 27.6% and SGPT in 29.3%).

Skin and subcutaneous tissue disorders
Very common: Alopecia, usually mild in nature, may occur (G3-4: 4.1% with Vinorelbine as single chemotherapeutic agent).
Rare: Generalized cutaneous reactions have been reported with Vinorelbine
Not known: Palmar-plantar erythrodysesthesia syndrome

Musculoskeletal and connective tissue disorders
Common: Arthralgia including jaw pain and myalgia

General disorders and administration site conditions
Very common: Reactions at the injection site may include erythema, burning pain, vein discoloration and local phlebitis (G 3-4: 3.7% with vinorelbine as single chemotherapeutic agent).
Common: Asthenia, fatigue, fever, pain at different locations including chest pain and pain at the tumour site have been experienced by patients receiving Vinorelbine therapy.
Rare: Local necrosis has been observed. Proper positioning of the intravenous needle or catheter and bolus injection followed by liberal flushing of the vein can limit these effects

Investigations
Common: Creatinine increased

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: http://www.hpra.ie/; E-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms
Overdosage with Vinorelbine could produce bone marrow hypoplasia (bone marrow hypoplasia which sometimes associated with the additional side effects infection, fever) and or paralytic ileus

Management
There is no known antidote for overdosage of Vinorelbine given intravenously, symptomatic measures are necessary in case of an overdosage, e.g.:- continuous control of vital signs and careful monitoring of the patient

- daily control of blood count to observe the need of blood transfusions, of growth factors and to detect the need of intensive care and to minimise the risk of infections
- measures for prevention or for therapy of paralytic ileus
- control of circulation system and of liver function
- broad spectrum antibiotic therapy may be necessary in case of complications due to infections

These measures should be instituted as deemed necessary by the physician.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Plant Alkaloids, Vinca alkaloids and analogues,
ATC code: LOlC A04

Vinorelbine concentrate for solution for infusion is a antineoplastic of the vinca alkaloid group.
The active substance Vinorelbine has as its molecular target the dynamic balance oftubulin/ microtubule. Vinorelbine prevents the polymerisation oftubulin. The activity is targeted mainly on mitotic microtubules; axonal microtubules are affected at high concentration.

The Vinorelbine spiralizing effect on tubulin is lower than that of vincristine. Vinorelbine inhibits the mitosis at phase G2-M and induces cell death at the interphase and at the following mitosis.

Safety and efficacy of Vinorelbine in paediatric patients have not been established. Clinical data from two single arm Phase II studies using intravenous Vinorelbine in 33 and 46 paediatric patients with recurrent solid tumours, including rhabdomyosarcoma, other soft tissue sarcoma, Ewing sarcoma, liposarcoma, synovial sarcoma, fibrosarcoma, central nervous system cancer, osteosarcoma, neuroblastoma at doses of 30 to 33.75 mg/m² D_1 and D_8 every 3 weeks or once weekly for 6 weeks every 8 weeks, showed no meaningful clinical activity. The toxicity profile was similar to that reported in adult patients. (See section 4.2)

5.2 Pharmacokinetic properties

After intravenous administration, Vinorelbine concentration in plasma is characterised by triphasic elimination. The terminal phase half-life in plasma is over 40 hours.

Pharmacokinetic parameters of vinorelbine were evaluated in blood.

Distribution
The steady-state volume of distribution is large, on average 22.2 l.kg-1 (range: 7.5-39.7 l.kg-1), which indicates extensive tissue distribution. Binding to plasma protein is low (13.5%). However, vinorelbine binds strongly to blood cells and especially to platelets. 78% of the total blood-bound vinorelbine was associated with platelets and 4.8% of the

total blood-bound vinorelbine was associated with lymphocytes. There is significant uptake of vinorelbine in the lungs, as assessed by surgical lung biopsies, which showed concentrations up to 300-fold higher than in serum. Vinorelbine is not found in the central nervous system.

Biotransformation
All metabolites of vinorelbine are formed by CYP 3A4 isoform of cytochromes P450, except 4-O-deacetylvinorelbine likely to be formed by carboxylesterases. 4-O-deacetylvinorelbine is the only active metabolite and the main one observed in blood.

Neither sulfate nor glucuronide conjugates are found.

Elimination
The mean terminal half-life of vinorelbine is around 40 hours. Blood clearance is high, approaching hepatic blood flow, and is 0.72 l/h/kg on average (range:0.32–1.26 l/h/kg).

Renal elimination is low (< 20% of the intravenous dose administered) and consists mostly in parent compound. Vinorelbine is eliminated primarily unchanged in the urine, only low deacetyl Vinorelbine concentrations have been recovered in humans. Biliary excretion is the predominant elimination route of unchanged vinorelbine, which is the main recovered compound, and its metabolites.

Special patient groups

Renal impairment
The effects of renal dysfunction on the pharmacokinetics of vinorelbine have not been studied. However, dose reduction in case of reduced renal function is not indicated due to the low renal elimination.

Liver impairment
A study has reported the effects of liver impairment on vinorelbine pharmacokinetics in patients with liver metastases due to breast cancer. From this study it was concluded that change in mean clearance of vinorelbine was only observed when more than 75% of the liver is involved.

Furthermore a phase I pharmacokinetic dose-adjusted study was conducted in cancer patients with liver dysfunction: 6 patients with moderate dysfunction (Bilirubin < 2 x UNL and Transaminases < 5 x UNL) treated up to 25 mg/m² and 8 patients with severe dysfunction (Bilirubin > 2 x UNL an/or Transaminases > 5 x UNL) treated up to 20 mg/m². Mean total clearance in these two subsets of patients was similar to that in patients with normal hepatic function therefore; the pharmacokinetics of vinorelbine is not modified in patients presenting moderate or severe liver impairment. Nevertheless, as a precautionary measure a reduced dose of 20mg/m² and close monitoring of haematological parameters is recommended in patient with severe liver impairment: see sections 4.2 and 4.4.

Elderly patients
A study with vinorelbine in elderly patients (≥70 years) with NSCLC demonstrated that pharmacokinetics of vinorelbine were not influenced by age. However, since elderly patients are frail, caution should be exercised when increasing the dose of vinorelbine see section 4.2.

Pharmacokinetic/pharmacodynamic relationships
A strong relationship has been demonstrated between vinorelbine blood exposure and of leucocytes or polymorphonuclear leucocytes decreases.

5.3 Preclinical safety data

Mutagenic and carcinogenic potential
In animal studies vinorelbine induced aneuploidy and polyploidy. Vinorelbine is assumed to cause mutagenic effects because of its interaction with the spindle apparates during mitosis. To avoid toxic effects in the carcinogenicty study Vinorelbine was administered only once every two weeks and no carcinogenic potential was seen.

Reproductive toxicity

In animal reproductive studies, effects were observed at subtherapeutic dosages. Embryo- and foetotoxicity were seen, such as intra-uterine growth retardation and delayed ossification.

Teratogenicity (fusion of the vertebrae, missing ribs) was observed at maternal toxic doses. In addition, spermatogenesis and secretion of prostate and seminal vesicles were reduced, but fertility in rats was not diminished.

Safety pharmacology
Bibliographic review concerning the tolerance of vinca alkaloids on the cardiovascular system shows the occurrence of some cardiac events (such as angina, myocardial infarction), but the incidence of these is low.
An ECG-study in dogs showed only some non-significant repolarisation-disturbances. A 39-week-study on primates showed no cardiovascular effects.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Vinorelbine concentrate for solution for infusion must not be diluted with alkaline solutions due to the risk of precipitation. In case of polychemotherapy Vinorelbine "Ebewe" should not be mixed with other agents.

Vinorelbine concentrate for solution for infusion must not be mixed with other preparations except with those mentioned in 6.6.

Vinorelbine "Ebewe" is not absorbed to or affected by either PVC, PE or clear neutral glass.

6.3 Shelf life

Unopened: 3 years

The product should be used immediately after opening

After Dilution:
Chemical and physical in-use stability has been demonstrated for 28 days when stored in a refrigerator (at 2-8^{o}C) or at room temperature and protected from light. Chemical and physical in-use stability has been demonstrated for 4 days when stored at room temperature without protection from light. See section 6.6 for the compatible diluents.
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8^{o}C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C). Keep the vials in the outer carton.

For in-use shelf-life details, please refer to section 6.3, Shelf-life.

6.5 Nature and contents of container

Glass vials (type 1). The stopper is covered with a crimped-on aluminium cap equipped with a polypropylene flip-off cap.

1ml & 5ml Vials packed in single cartons

Not all vial sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

The preparation and administration of vinorelbine should be carried out by trained staff and as with all cytotoxic agents; precautions should be taken to avoid exposing staff during pregnancy. Preparation of solution for administration should be carried out in a designated handling area and working over a washable tray or disposable plastic-backed absorbent paper.Suitable eye protection, disposable gloves, face mask and disposable apron should be worn. Eventual spillage or leakage should be mopped up.Care must be taken to avoid product contamination of the eye thereby causing severe irritation or even corneal ulcer. If exposure occurs, the eyes should immediately be thoroughly flushed with physiologic sodium chloride 9 mg/ml (0.9%) solution for 15 minutes. On completion, any exposed surface should be thoroughly cleaned and hands and face washed.

It is recommended to infuse vinorelbine over 6-10 minutes after dilution in 20−50 ml of sodium chloride 9 mg/ml (0.9%) solution for injection or in glucose solution for injection 5%. After administration the vein should be thoroughly flushed with at least 250 ml of isotonic solution.
Vinorelbine must be given strictly intravenously: it is very important to make sure that the cannula is accurately placed in the vein before starting to infuse vinorelbine. If the drug extravasates into the surrounding tissue during the administration considerable local irritation may occur. In this case, the administration should be stopped, the vein flushed with normal saline and the remaining dose administered in another vein.
In case of extravasations, to reduce the risk of phlebitis IV glucocorticoids could be administered immediately.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Fannin Limited
Fannin House
South County Business Park
Leopardstown
Dublin 18
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 1457/004/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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