Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Neotigason 10 mg capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Capsules containing 10 mg of acitretin.
Excipients: Glucose 16.40 mg

For the full list of excipients, *see section 6.1*.

3 PHARMACEUTICAL FORM

Capsule, hard.
Capsule with a brown cap and white body with '10' printed in black on the body; capsule size 4.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Severe extensive psoriasis which is resistant to other forms of therapy.

Palmo-plantar pustular psoriasis.

Severe congenital ichthyosis.

Severe Darier's disease (keratosis follicularis).

Severe lichen planus.

4.2 Posology and method of administration

Posology
Neotigason should only be prescribed by physicians who are experienced in the use of systemic retinoids and understand the risk of teratogenicity associated with acitretin therapy. See Section 4.4 and 4.6.

Neotigason capsules are for oral administration.
The capsules should be taken once daily with meals or with milk.

There is wide variation in the absorption and rate of metabolism of Neotigason. This necessitates individual adjustment of dosage. For this reason the following dosage recommendations can serve only as a guide.

Adults
Initial daily dose should be 25 mg or 30 mg for two to four weeks. After this initial treatment period, the involved areas of the skin should show a marked response and/or side effects should be apparent. Following assessment of the initial treatment period, titration of the dose upwards or downwards may be necessary to increase the therapeutic effect. In general, a daily dosage of 25-50 mg taken for a further six to eight weeks achieves optimal therapeutic results. However, it may be necessary in some cases to increase the dose up to a maximum of 75 mg/day.

Therapy can be discontinued in patients with psoriasis whose lesions have improved sufficiently. Relapses should be treated as described above.

Patients with severe congenital ichthyosis and severe Darier's disease and severe lichen planus may require therapy beyond three months. The lowest effective dosage, not exceeding 50 mg/day, should be given.

In patients with Darier's disease a starting dose of 10 mg may be appropriate. The dose should be increased cautiously as isomorphic reactions may occur.

Continuous use beyond 6 months is contra-indicated as only limited clinical data are available on patients treated beyond this length of time.

Elderly
Dosage recommendations are the same as for other adults.

Paediatric population
In view of possible severe side-effects associated with long-term treatment, Neotigason is contra-indicated in children unless, in the opinion of the physician, the benefits significantly outweigh the risks.

The dosage should be established according to bodyweight. The daily dosage is about 0.5mg/kg. Higher doses (up to 1mg/kg daily) may be necessary in some cases for limited periods, but only up to a maximum of 35mg/day. The maintenance dose should be kept as low as possible in view of possible long-term side-effects.

Combination therapy
Other dermatological therapy, particularly with keratolytics, should normally be stopped before administration of Neotigason. However, the use of topical corticosteroids or bland emollient ointment may be continued if indicated.

When Neotigason is used in combination with other types of therapy, it may be possible, depending on the individual patients response, to reduce the dosage of Neotigason.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1 or to other retinoids.

Neotigason is a powerful human teratogen and it is strictly contraindicated in pregnant women and women of childbearing potential unless all the conditions of the Pregnancy Prevention Programme are met (see section 4.4).

Breast feeding.

Severely impaired liver function.

Severely impaired kidney function.

Chronic abnormally elevated blood lipid values.

Since both Neotigason and tetracyclines can cause increased intracranial pressure, their combined use is contraindicated (see section 4.5).

An increased risk of hepatitis has been reported to result from combined use of methotrexate and etretinate. Consequently, the combination of methotrexate with Neotigason is also contraindicated (see section 4.5).

Concomitant administration of Neotigason and vitamin A or other retinoids is contraindicated due to the risk of hypervitaminosis A (see section 4.5).

4.4 Special warnings and precautions for use

Teratogenic effects
Neotigason is a powerful human teratogen inducing a high frequency of severe and life threatening birth defects.

Neotigason is strictly contraindicated in:
- Pregnant women
- Women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme are met

Pregnancy Prevention Programme
This medicinal product is TERATOGENIC.
Acitretin is contraindicated in women of childbearing potential unless all of the following conditions of the Pregnancy Prevention Programme are met:

- She has extensive psoriasis which is resistant to other forms of therapy. Palmo-plantar pustular psoriasis. Severe congenital ichthyosis. Severe Darier's disease (keratosis follicularis). Severe lichen planus (see section 4.1, "Therapeutic indications").
- The potential for pregnancy must be assessed for all female patients.
- She understands the teratogenic risk.
- She understands the need for rigorous follow-up on a monthly basis.
- She understands and accepts the need for effective contraception, without interruption, 1 month before starting treatment, throughout the entire duration of treatment and for 3 years after the end of treatment. At least one highly effective method of contraception (i.e. a user-independent form) or two complementary user-dependent forms of contraception should be used.
- Individual circumstances should be evaluated in each case, when choosing the contraception method, involving the patient in the discussion, to guarantee her engagement and compliance with the chosen measures.
- Even if she has amenorrhea she must follow all the advice on effective contraception.
- She is informed and understands the potential consequences of pregnancy and the need to rapidly consult if there is a risk of pregnancy or if she might be pregnant.
- She understands the need and accepts to undergo regular pregnancy testing before, ideally monthly during treatment and periodically with 1-3 monthly intervals for a period of 3 years after stopping treatment.
- She has acknowledged that she has understood the hazards and necessary precautions associated with the use of acitretin.

These conditions also concern women who are not currently sexually active unless the prescriber considers that there are compelling reasons to indicate that there is no risk of pregnancy.

The prescriber must ensure that:

- The patient complies with the conditions for pregnancy prevention as listed above, including confirmation that she has an adequate level of understanding.
- The patient has acknowledged the aforementioned conditions.
- The patient understands that she must consistently and correctly use one highly effective method of contraception (i.e. a user-independent form) or two complementary user-dependent forms of contraception, for at least 1 month prior to starting treatment and is continuing to use effective contraception throughout the treatment period and for at least 3 years after cessation of treatment.
- Negative pregnancy test results have been obtained before, during and periodically with 1-3 monthly intervals for a period of 3 years after stopping treatment. The dates and results of pregnancy tests should be documented.

If pregnancy occurs in a woman treated with acitretin, treatment must be stopped and the patient should be referred to a physician specialised or experienced in teratology for evaluation and advice.

If pregnancy occurs after stopping treatment there remains a risk of severe and serious malformation of the foetus. This risk persists until the product has been completely eliminated, which is within 3 years following the end of treatment.

Contraception
Female patients must be provided with comprehensive information on pregnancy prevention and should be referred for contraceptive advice if they are not using effective contraception. If the prescribing physician is not in a position to provide

such information the patient should be referred to the relevant healthcare professional.

As a minimum requirement, female patients of childbearing potential must use at least one highly effective method of contraception (i.e. a user-independent form), or two complementary user-dependent forms of contraception. Contraception should be used for at least 1 month prior to starting treatment, throughout treatment and continue for at least 3 years after stopping treatment with acitretin, even in patients with amenorrhea.

Individual circumstances should be evaluated in each case, when choosing the contraception method involving the patient in the discussion, to guarantee her engagement and compliance with the chosen measures.

Pregnancy testing
According to local practice, medically supervised pregnancy tests with a minimum sensitivity of 25mUI/mL are recommended to be performed, as follows.

Prior to starting therapy
At least one month after the patient has started using contraception, and shortly (preferably a few days) prior to the first prescription, the patient should undergo a medically supervised pregnancy test. This test should ensure the patient is not pregnant when she starts treatment with acitretin.

Follow-up visits

Follow-up visits should be arranged at regular intervals, ideally monthly. The need for repeated medically supervised pregnancy tests every month should be determined according to local practice including consideration of the patient's sexual activity, recent menstrual history (abnormal menses, missed periods or amenorrhea) and method of contraception. Where indicated, follow-up pregnancy tests should be performed on the day of the prescribing visit or in the 3 days prior to the visit to the prescriber.

End of treatment

Women should undergo pregnancy test periodically with 1-3 monthly intervals for a period of 3 years after stopping treatment.

Prescribing and dispensing restrictions
For women of childbearing potential, the prescription duration of Neotigason should ideally be limited to 30 days in order to support regular follow up, including pregnancy testing and monitoring. Ideally, pregnancy testing, issuing a prescription and dispensing of Neotigason should occur on the same day.

This monthly follow-up will allow ensuring that regular pregnancy testing and monitoring is performed and that the patient is not pregnant before receiving the next cycle of medication.

Male patients
The available data suggest that the level of maternal exposure from the semen of the patients receiving Neotigason is not of a sufficient magnitude to be associated with the teratogenic effects of Neotigason. Male patients should be reminded that they must not share their medication with anyone, particularly not females.

Additional precautions
Patients should be instructed never to give this medicinal product to another person and to return any unused capsules to their pharmacist at the end of treatment.

Patients should not donate blood during therapy and for 3 years following discontinuation of acitretin because of the potential risk to the foetus of a pregnant transfusion recipient.

Educational material
In order to assist prescribers, pharmacists and patients in avoiding foetal exposure to acitretin the Marketing Authorisation Holder will provide educational material to reinforce the warnings about the teratogenicity of acitretin, to provide advice on contraception before therapy is started and to provide guidance on the need for pregnancy testing.

Full patient information about the teratogenic risk and the strict pregnancy prevention measures as specified in the Pregnancy Prevention Programme should be given by the physician to all patients, both male and female.

Psychiatric disorders
Depression, depression aggravated, anxiety, mood alterations and psychotic disorder have been reported in patients treated with systemic retinoids, including acitretin. Particular care should be taken in patients with a history of depression. Patients should be monitored for signs of depression and referred for appropriate treatment if necessary. Awareness by family or friends may be useful to detect mental health deterioration.

Clinical evidence has shown that etretinate can be formed with concurrent ingestion of Neotigason and alcohol. Etretinate is highly teratogenic and has a longer half-life (approximately 120 days) than acitretin. Women of childbearing age must therefore not consume alcohol (in drinks, food or medicines) during treatment with acitretin and for 2 months after cessation of Neotigason therapy.

Hepatic function should be checked before starting treatment with Neotigason, every 1-2 weeks for the first 2 months after commencement and then every 3 months during treatment. If abnormal results are obtained, weekly checks should be instituted. If hepatic function fails to return to normal or deteriorates further, Neotigason must be withdrawn. In such cases it is advisable to continue monitoring hepatic function for at least 3 months (see section 4.8).

Serum cholesterol and serum triglycerides (fasting values) must be monitored before starting treatment, one month after commencement and then every 3 months during treatment. Acitretin treatment should be discontinued in case of uncontrolled levels of hypertriglyceridemia or if symptoms of pancreatitis occur.

Decreased night vision has been reported with Neotigason therapy. Patients should be advised of this potential problem and warned to be cautious when driving or operating any vehicle at night. Visual problems should be carefully monitored (see section 4.8).

There have been rare reports of benign intracranial hypertension. Patients with severe headache, nausea, vomiting, and visual disturbances should discontinue Neotigason immediately and be referred for neurologic evaluation and care (see section 4.8).

In adults, especially elderly, receiving long-term treatment with Neotigason, appropriate examinations should be periodically performed in view of possible ossification abnormalities (see section 4.8). If such disorders arise, the continuation of therapy should be discussed with the patient on the basis of a careful risk/benefit analysis.

There have been occasional reports of bone changes in children, including premature epiphyseal closure, skeletal hyperostosis and extraosseous calcification after long-term treatment with etretinate, these effects may be expected with Neotigason. Therefore, in children growth parameters and bone development must be closely monitored.

It should be emphasized that, at the present time, not all the consequences of life-long administration of acitretin are known.

The effects of UV light are enhanced by retinoid therapy; therefore patients should avoid excessive exposure to sunlight and the unsupervised use of sun lamps. Where necessary a sun-protection product with a high protection factor of at least SPF 15 should be used.

Acitretin has been shown to affect diaphyseal and spongy bone adversely in animals at high doses in excess of those recommended for use in man. Since skeletal hyperostosis and extraosseous calcification have been reported following long-term treatment with etretinate in man, this effect should be expected with acitretin therapy.

Since there have been occasional reports of bone changes in children, this effect may be expected with acitretin. Long-term therapy in children is not, therefore, recommended. If, in exceptional circumstances, such therapy is undertaken the child should be carefully monitored for any abnormalities of musculo-skeletal development.

In the treatment of ichthyosis or Darier's disease in which continuous therapy with acitretin may be necessary, patients should have a base line x-ray of thoracic spine (adults) or the forearm and hand (children) prior to and periodically during treatment.

Dryness of the conjunctivae may lead to mild-to-moderate conjunctivitis or xerophthalmia and result in intolerance of contact lenses; it may be alleviated by lubrication with artificial tears or topical antibiotics (see section 4.8).

Patients should be warned of the possibility of hair thinning and alopecia occurring. These are usually noted 4 to 8 weeks after starting therapy, and are reversible following discontinuation of Neotigason. Full recovery usually occurs within 6 months of stopping treatment in the majority of patients (see section 4.8 Undesirable effects).

High risk patients:
In patients with diabetes, alcoholism, obesity, cardiovascular risk factors or a lipid metabolism disorder undergoing treatment with Neotigason, more frequent checks are necessary of serum values for lipids, and/or glycaemia and other cardiovascular risk indictors, e.g. blood pressure.
In diabetics, retinoids can either improve or worsen glucose tolerance. Blood-sugar levels must therefore be checked more frequently than usual in the early stages of treatment.
For all high risk patients where cardiovascular risk indicators fail to return to normal or deteriorate further, dose reduction or withdrawal of Neotigason should be considered.

Very rare cases of Capillary Leak Syndrome / retinoic acid syndrome have been reported from world-wide post marketing experience.

Very rare cases of exfoliative dermatitis have been reported from world-wide post marketing experience.

Excipients

Glucose
Patients with rare glucose-galactose malabsorption should not take this medicine.

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant administration of methotrexate, tetracyclines or vitamin A and other retinoids with acitretin is contraindicated, see section 4.3.

Low dose progesterone-only products (minipills) may be an inadequate method of contraception during acitretin therapy, see section 4.4. Interactions with combined estrogen/progestogen oral contraceptives have not been observed.

In a study with healthy volunteers, concurrent intake of a single dose of acitretin together with alcohol led to the formation of etretinate which is highly teratogenic. The mechanism of this metabolic process has not been defined, so it is not clear whether other interacting agents are also possible.

Women of childbearing age must therefore not consume alcohol (in drinks, food or medicines) during treatment with acitretin and for 2 months after cessation of acitretin therapy. (see section 4.4 and 5.2).

If Neotigason is given concurrently with phenytoin, it must be remembered that Neotigason partially reduces phenytoin's protein binding. The clinical significance of this is as yet unknown.

Further interactions between Neotigason and other substances (e.g. digoxin, cimetidine) have not been observed so far.

Investigations into the effect of Neotigason on the protein binding of anticoagulants of the coumarin type (warfarin) revealed no interaction.

Etretinate formation without concurrent alcohol intake cannot be excluded. Therefore, since the elimination half-life of etretinate is 120 days, contraceptive measures and pregnancy testing in women of childbearing potential must be undertaken for 3 years after completion of acitretin treatment (see section 4.4 Special warnings and special precautions for use).

An increased risk of hepatitis has been reported following the concomitant use of methotrexate and etretinate. Consequently, the concomitant use of methotrexate and Neotigason should be avoided (see section 4.3 Contra-indications).

Concomitant administration of vitamin A and other retinoids must be avoided because of the risk of hypervitaminosis A (see section 4.3).

Since both Neotigason and tetracyclines can cause increased intracranial pressure, their combined use is contraindicated (see section 4.3).

4.6 Fertility, pregnancy and lactation

Teratogenic effects
Neotigason is a powerful human teratogen inducing a high frequency of severe and life threatening birth defects.

Neotigason is strictly contraindicated in:
- Pregnant women
- Women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme are met

See section 4.4 'Special warnings and precautions for use' for further information.

Should pregnancy occur there is a high risk of severe malformation of the foetus (e.g. craniofacial defects, cardiac and vascular or CNS malformations, skeletal and thymic defects) and the incidence of spontaneous abortion is increased.

Pregnancy
Neotigason is contraindicated in pregnant women (see section 4.3).

Breastfeeding
Neotigason must not be given to nursing mothers (see section 4.3).

4.7 Effects on ability to drive and use machines

Decreased night vision has been reported with Neotigason therapy. Patients should be advised of this potential problem and warned to be cautious when driving or operating any vehicle at night. Visual problems should be carefully monitored (see section *4.8 Undesirable effects*).

4.8 Undesirable effects

Undesirable effects are seen in most patients receiving Neotigason. However, they usually disappear when the dosage is reduced or the drug is withdrawn. An initial worsening of psoriasis symptoms is sometimes seen at the beginning of the treatment period.

The most frequent undesirable effects observed are symptoms of hypervitaminosis A, e.g. dryness of the lips, which can be alleviated by application of a fatty ointment.

Undesirable effects reported for acitretin in clinical trials or as post-marketing events are listed below by System Organ Class and frequency. Frequencies are defined as:

Very common (≥1/10)
Common (≥1/100 to <1/10)
Uncommon (≥1/1,000 to <1/100)
Rare (≥1/10,000 to <1/1,000)
Very rare (<1/10,000)
Not known (cannot be estimated from the available data)

Infections and infestations Very rare	Vulvo-vaginitis due to *Candida albicans*
Immune system disorders	Type I hypersensitivity

Frequency not known	
Psychiatric disorders Frequency not known	Alteredmood, psychotic disorder
Nervous system disorders Common Uncommon Rare Very rare	Headache Dizziness Neuropathy peripheral Benign intracranial hypertension (see section 4.4), paraesthesia, somnolence
Eye disorders Very common Uncommon Very rare	Drying of and inflammation of mucous membranes (e.g. conjunctivitis, xerophthalmia), which may lead to intolerance of contact lenses Vision blurred Night blindness (see section 4.4), ulcerative keratitis
Ear and labyrinth disorders Frequency not known	Hearing impaired, tinnitus
Vascular disorders Common	Flushing , Capillary Leak Syndrome/retinoic acid syndrome[6]
Respiratory, thoracic and mediastinal disorders Very common Not Known	 Drying of and inflammation of mucous membranes (e.g. epistaxis and rhinitis) Dysphonia
Gastrointestinal disorders Very Rare Very common Common Uncommon Frequency not known	Pancreatitis Dry mouth, thirst, dry lip Stomatitis, gastro-intestinal disorders (e.g. abdominal pain, diarrhoea, nausea, vomiting), Gingivitis Dysgeusia, rectal haemorrhage
Hepatobiliary disorders Uncommon Very rare	Hepatitis Jaundice
Skin and subcutaneous tissue disorders Very common Common	Cheilitis, pruritus, alopecia, skin exfoliation (all over the body, particularly on the palms and soles), skin atrophy Skin fragility, sticky skin, dermatitis, hair texture abnormal, brittle nails, paronychia, erythema, onychoclasis, hyperhydrosis,

Uncommon Frequency not known	Rhagades, dermatitis bullous, photosensitivity reaction Pyogenic granuloma, madarosis, angioedema, urticaria, exfoliative dermatitis, thinning of skin
Musculoskeletal and connective tissue disorders Common Very rare	Arthralgia, myalgia Bone pain, exostosis (maintenance treatment may result in progression of existing spinal hyperostosis, in appearance of new hyperostotic lesions and in extraskeletal calcification, as has been observed in long-term systemic treatment with retinoids) (see section 4.4)
General disorders and administration site conditions Common Very rare	Peripheral oedema Granuloma, malaise
Investigations Very common	Liver function test abnormal (transient, usually reversible elevation of transaminases and alkaline phosphatises) (see section 4.4) Lipids abnormal (during treatment with high doses of acitretin, reversible elevation of serum triglycerides and serum cholesterol has occurred, especially in high-risk patients and during long-term treatment (see section 4.4). An associated risk of atherogenesis cannot be ruled out if these conditions persist)

Children
There have been occasional reports of bone changes in children, including premature epiphyseal closure, skeletal hyperostosis and extraosseous calcification after long-term treatment with etretinate, these effects may be expected with acitretin. In children, growth parameters and bone development must be closely monitored.

Diabetics
Retinoids can either improve or worsen glucose tolerance (see section 4.4).

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, Website: www.hpra.ie.

4.9 Overdose

In the event of acute overdose, Neotigason must be withdrawn at once. Symptoms of overdose are identical to an acute hypervitaminosis A, i.e. headache, vertigo, nausea or vomiting, drowsiness, irritability and pruritus. Specific treatment is unnecessary because of the low acute toxicity of the preparation.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: D05BB02
Retinol (Vitamin A) is known to be essential for normal epithelial growth and differentiation, though the mode of this effect is not yet established. Both retinol and retinoic acid are capable of reversing hyperkeratotic and metaplastic skin changes. However, these effects are generally only obtained at dosages associated with considerable local or systemic toxicity.

Acitretin, a synthetic aromatic derivative of retinoic acid, has a favourable therapeutic ratio, with a greater and more specific inhibitory effect on psoriasis and disorders of epithelial keratinisation. The usual therapeutic response to acitretin consists of desquamation (with or without erythema) followed by more normal re-epithelialisation.

Acitretin is the main active metabolite of etretinate (Tigason).

5.2 Pharmacokinetic properties

Absorption
Acitertin reaches peak plasma concentration 1-4 hours after ingestion of the drug. Bioavailability of orally administered acitretin is enhanced by food. Bioavailability of a single dose is approximately 60%, but inter-patient variability is considerable (36-95%).

Distribution
Acitretin is highly lipophilic and penetrates readily into body tissues. Protein binding of acitretin exceeds 99%. In animal studies, acitretin passed the placental barrier in quantities sufficient to produce sufficient to produce foetal malformations. Due to its lipophilic nature, it can be assumed that acitretin passes into breast milk in considerable quantities.

Metabolism
Acitretin is metabolised by isomerisation into its 13-cis isomer (cis acitretin), by glucuronidation and cleavage of the side chain.

Elimination
Multiple-dose studies in patients aged 21-70 years showed an elimination half-life of approximately 50 hours for acitretin and 60 hours for its main metabolite in plasma, cis acitretin, which is also a teratgen. From the longest elimination half-life observed in these patents for acitretin (96 hours) and cis acitretin (123 hours), and assuming linear kinetics, it can be predicted that more than 99% of the drug is eliminated within 36 days after cessation of long-term kinetics, it can be predicted that more than 99% of the drug is eliminated within 36 days after cessation of long-term therapy. Furthermore, plasma concentrations of acitretin and cis acitretin dropped below the sensitivity limit of the assay (<6ng/ml) within 36 days following cessation of treatment. Acitretin is excreted entirely in the form of its metabolites, in approximately equal parts via the kidneys and the bile.

NOTE:
Clinical evidence has shown that etretinate can be formed with concurrent ingestion of acitretin and alcohol.Therefore, since etretinate is highly teratogenic and the elimination half-life of etretinate is approximately 120 days, pregnancy testing and contraceptive measures must be taken for 3 years after completion of acitretin treatment (see section 4.4 and 4.5).

5.3 Preclinical safety data

None stated.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content:
Glucose, liquid, spray-dried
Sodium ascorbate
Gelatin
Microcrystalline cellulose

Capsule shell:
Gelatin
Iron oxide black (E172)
Iron oxide yellow (E172)
Iron oxide red (E172)
Titanium dioxide (E171)

Printing ink:
Shellac
Propylene glycol
Ammonium hydroxide
Iron oxide black (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C.

Store in the original package to protect from moisture.

6.5 Nature and contents of container

All aluminium blisters and PVC/PVDC or PVC/PE/PVDC blisters with aluminium cover foil containing 56 or 60 capsules.
Not all pack 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

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Teva B.V.
Swensweg 5
2031GA Haarlem
Netherlands

8 MARKETING AUTHORISATION NUMBER

PA1986/113/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 16 June 2007

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