Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Ternaf 250 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 250 mg terbinafine as terbinafine hydrochloride.

For the full list of excipients,see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White or almost white, round, scored on both sides, convex tablets, coded "TER 250" on one side.

The tablet can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of terbinafine sensitive fungal infections such as Tinea corporis, Tinea cruris and Tinea pedis (caused by Dermatophytes see section 5.1) is considered appropriate due to the site, severity or extent of the infection.

The treatment of onychomycosis (terbinafine-sensitive fungal infection of the nails) caused by dermatophytes.

Consideration should be given to national recommendations on the appropriate use and prescription of antifungal agents.

Note: In contrast to topical terbinafine, oral terbinafine is not effective in pityriasis versicolor and vaginal candidiasis.

4.2 Posology and method of administration

Posology
Adults
250 mg once daily

The duration of treatment varies according to the indication and the severity of the infection.

Skin infections
The likely durations of treatment for Tinea corporis and Tinea cruris are 2-4 weeks. For Tinea pedis (interdigital, plantar/moccasin-type): recommended treatment periods may be up to 6 weeks.

Onychomycosis
The duration of treatment (finger & toe nails) for most patients is between 6 weeks and 3 months. In the treatment of toenail infections, 3 months is usually sufficient although a few patients may require treatment of 6 months or longer. Poor nail outgrowth during the first weeks of treatment may enable identification of those patients in whom longer therapy is required.

Complete resolution of the signs and symptoms of infection may not occur until several weeks after mycological cure, and is only seen several months after stopping treatment, which is the time for outgrowth of a healthy nail.

Additional information on special population
Liver impairment
Terbinafine tablets are not recommended for patients with chronic or active hepatic disease (see sections 4.3 and 4.4.

Renal impairment

The use of terbinafine tablets has not been adequately studied in patients with renal impairment and is therefore not recommended in this population (see sections 4.4 and 5.2)

Elderly people
There is no evidence to suggest that older patients (aged 65 years and above) require different dosages or experience different side effects than younger patients. When prescribing terbinafine tablets for patients in this age group, the possibility of pre-existing impairment of hepatic or kidney function should be considered (see sections 4.3, 4.4 and 4.8).

Paediatric population
There is no experience on the use of terbinafine in children, for that use is not recommended in this population.

Method of administration
Oral use.

The tablets are taken orally with water. They should preferably be taken at the same time each day and can be taken on an empty stomach or after a meal. The bioavailability of terbinafine is not influenced by food intake.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Severe hepatic impairment.

4.4 Special warnings and precautions for use

Liver function
Terbinafine tablets are not recommended for patients with chronic or active hepatic disease. Before prescribing terbinafine tablets, liver function tests should be performed since hepatotoxicity may occur in patients with and without pre-existing hepatic disease. Therefore, periodic monitoring (after 4-6 weeks of treatment) of liver function test is recommended. Terbinafine should be immediately discontinued in case of elevation of liver function test. Very rare cases of serious hepatic failure (some with a fatal outcome, or requiring hepatic transplant) have been reported in patients treated with terbinafine tablets. In the majority of hepatic failure cases the patients had serious underlying systemic conditions (see sections 4.3 and see section 4.8).

Patients prescribed terbinafine tablets should be warned to report immediately any signs and symptoms of unexplained persistent nausea, decreased appetite, fatigue, vomiting, right upper abdominal pain, or jaundice, dark urine or pale faeces. Patients with these symptoms should discontinue taking oral terbinafine and the patient's hepatic function should be immediately evaluated.

Dermatological effects
Serious skin reactions (e.g. Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms [DRESS]) have been very rarely reported in patients taking terbinafine tablets. If progressive skin rash occurs, treatment with terbinafine tablets should be discontinued.

Terbinafine should be used with caution in patients with pre-existing psoriasis or lupus erythematosus as precipitation and exacerbation of psoriasis and cutaneous and systemic lupus erythematosus have been reported in a post marketing setting.

Haematological effects
Very rare cases of blood disorders (neutropenia, agranulocytosis, thrombocytopenia, pancytopenia) have been reported in patients treated with terbinafine tablets. Aetiology of any blood disorders that occur in patients treated with terbinafine tablets should be evaluated and consideration should be given for a possible change in medication regimen, including discontinuation of treatment with terbinafine tablets.

Renal function
In patients with renal impairment (creatinine clearance less than 50 ml/min or serum creatinine of more than 300 micro mol/l) the use of terbinafine tablets has not been adequately studied, and therefore, is not recommended (see section 5.2).

Interactions
In vitro and *in vivo* studies have shown that terbinafine inhibits the CYP2D6 metabolism (see section 4.5).

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

4.5 Interaction with other medicinal products and other forms of interactions

Effect of other medicinal products on terbinafine
The plasma clearance of terbinafine may be accelerated by drugs, which induce metabolism and may be inhibited by drugs, which inhibit cytochrome P450. Where co-administration of such agents is necessary, the dosage of terbinafine tablets may need to be adjusted accordingly.

The following medicinal products may increase the effect or plasma concentration of terbinafine

- **Cimetidine** decreased the clearance of terbinafine by 33%.
- **Fluconazole** increased the C_{max} and AUC of terbinafine by 52% and 69% respectively, due to inhibition of both CYP2C9 and CYP3A4 enzymes. Similar increase in exposure may occur when other drugs which inhibit both CYP2C9 and CYP3A4 such as **ketoconazole** and **amiodarone** are concomitantly administered with terbinafine.

The following medicinal products may decrease the effect or plasma concentration of terbinafine

- **Rifampicin** increased the clearance of terbinafine by 100%.

Effect of terbinafine on other medicinal products
Terbinafine may increase the effect or plasma concentration of the following medicinal products

- Terbinafine decreased the clearance of **caffeine** administered intravenously by 19%.
- **Compounds predominantly metabolised by CYP2D6**

In vitro and *in vivo* studies have shown that terbinafine inhibits the CYP2D6-mediated metabolism. This finding may be of clinical relevance for compounds predominantly metabolised by CYP2D6, e.g. certain members of the following drug classes, tricyclic antidepressants (TCAs), beta-blockers, selective serotonine reuptake inhibitors (SSRIs), antiarrhythmics (including class 1A, 1B and 1C) and monoamine oxidase inhibitors (MAO-Is) Type B, especially if they also have a narrow therapeutic window (see section 4.4).

Terbinafine decreased the clearance of **desipramine** by 82% (see section 4.4).

In studies in healthy subjects characterised as extensive metabolisers of **dextromethorphan** (antitussive drug and CYP2D6 probe substrate), terbinafine increased the dextromethorphan/dextrorphan metabolic ratio in urine by 16- to 97-fold on average. Thus, terbinafine may convert extensive CYP2D6 metabolisers to poor metaboliser status.

Information on other drugs concomitantly used with terbinafine resulting in no or negligible interactions
According to the results from studies undertaken *in vitro* and in healthy volunteers, terbinafine shows negligible potential to inhibit or induce the clearance of most drugs that are metabolised via the cytochrome P450 system (e.g. terfenadine, triazolam, tolbutamide or oral contraceptives) with exception of those metabolised through CYP2D6 (see above).

Terbinafine does not interfere with the clearance of antipyrine or digoxin.

There was no effect of terbinafine on the pharmacokinetics of fluconazole. Further there was no clinically relevant interaction between terbinafine and the potential comedications cotrimoxazole (trimethoprim and sulfamethoxazole), zidovudine or theophylline.

Some cases of menstrual disturbance (such as irregular cycle, breakthrough bleeding, intermenstrual bleeding, amenorrhoea) have been reported in patients taking terbinafine tablets concomitantly with **oral contraceptives**, although the incidence of these disorders remains within the background incidence of patients taking oral contraceptives alone.

Terbinafine may decrease the effect or plasma concentration of the following medicinal products

- Terbinafine increased the clearance of **ciclosporin** by 15%.

Rare cases of changes in INR and/or prothrombin time have been reported in patients receiving terbinafine concomitantly with **warfarin**.

4.6 Fertility, pregnancy and lactation

Pregnancy
Foetal toxicity studies in animals suggest no adverse effects. Since clinical experience in pregnant women is very limited, terbinafine tablets should not be used during pregnancy unless clinical condition of the woman requires treatment with oral terbinafine and the potential benefits for the mother outweigh any potential risks for the foetus.

Breast-feeding
Terbinafine is excreted in breast milk; mothers receiving oral treatment with terbinafine should therefore not breast-feed.

Fertility
There is no relevant information from human experience. Fertility studies in rats suggest no adverse effects (see section 5.3).

4.7 Effects on ability to drive and use machines

No studies on the effects of terbinafine tablets treatment on the ability to drive and use machines have been performed. Patients who experience dizziness as an undesirable effect should avoid driving vehicles or using machines.

4.8 Undesirable effects

Adverse drug reactions from clinical trials or post-marketing experience are listed by MedDRA system organ class. Within each system organ class, the adverse drug reactions are ranked by frequency, with the most frequent reactions first. Within each frequency grouping, adverse drug reactions are presented in order of decreasing seriousness.
The corresponding frequency category for each adverse drug reaction is based on the following convention:
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)

System Organ Class	**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)	**Frequency not known** (cannot be estimated from the available data)*
Blood and lymphatic system disorders			Anemia		Neutropenia, Agranulocytosis, Thrombocytopenia, Pancytopenia (See section 4.4)	
Immune system disorders					Anaphylactoid reaction Angioedema Cutaneous and systemic lupus erythematosus	Anaphylactic reaction, Serum sickness-like reaction
Metabolism and nutrition disorders	Decreased appetite					
Psychiatric disorders		Depression	Anxiety			Depressive symptoms secondary to dysgeusia
Nervous system disorders	Headache	Dysgeusia including ageusia** Dizziness	Paraesthesia Hypoaesthesia			Anosmia including permanent anosmia, Hyposmia
Eye disorders		Visual impairment				Vision blurred, visual acuity reduced

System Organ Class	**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)	**Frequency not known** (cannot be estimated from the available data)*
Ear and labyrinth disorders			Tinnitus			Hypoacusis, Hearing impaired
Vascular disorders						Vasculitis
Gastrointestinal disorders	Abdominal distension Dyspepsia Nausea Abdominal pain Diarrhoea					Pancreatitis
Hepatobiliary disorders				Hepatic failure Hepatitis Jaundice Cholestasis Hepatic enzymes increased (see section 4.4)	Liver failure with subsequent liver transplant or death. In the majority of these cases the patients had serious underlying diseases.	
Skin and subcutaneous tissue disorders	Rash Urticaria		Photosensitivity reactions (e.g. photodermatosis, photosensitivity allergic reaction and polymorphic light eruption)		Erythema multiforme Stevens Johnson syndrome Toxic epidermal necrolysis Acute generalized exanthematous pustulosis (AGEP) Toxic skin eruption Dermatitis exfoliative, Dermatitis bullous Psoriasiform eruptions or exacerbation of psoriasis Alopecia	Drug rash with eosinophilia and systemic symptoms (DRESS)
Musculo-skeletal, connective tissue and bone disorders	Arthralgia Myalgia					Rhabdomyolysis
General disorders and administra-tion site conditions		Fatigue	Pyrexia			Influenza-like illness
Investigations			Weight decreased***			Blood creatine phosphokinase increased

* The following adverse drug reactions have been derived from post-marketing experience with terbinafine via spontaneous case reports and literature cases. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency which is therefore categorized as not known.

** Dysgeusia, including ageusia, which usually recover within several weeks after discontinuation of the drug. Isolated cases of prolonged hypogeusia have been reported.
*** Weight decreased secondary to dysgeusia.

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

A few cases of overdose (up to 5 g) have been reported, giving rise to headache, nausea, upper abdominal pain and dizziness. The recommended treatment of overdose consists of eliminating the drug, primarily by the administration of activated charcoal, and giving symptomatic supportive therapy, if needed.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Dermatologicals, antifungals for systemic use.
ATC code: D01BA02

Mechanism of action
Terbinafine interferes specifically with fungal sterol biosynthesis at an early step. This leads to a deficiency in ergosterol and to an intracellular accumulation of squalene, resulting in fungal cell death. Terbinafine acts by inhibition of squalene epoxidase in the fungal cell membrane.

Pharmacodynamic effects
Terbinafine is an allylamine which has a broad spectrum of activity against fungal pathogens of the skin, hair and nails including dermatophytes such as Trichophyton (e.g. T. rubrum, T. mentagrophytes, T. verrucosum, T. tonsurans, T. violaceum), Microsporum (e.g. M. canis), Epidermophyton floccosum, and yeasts of the genera Candida (e.g. C. albicans) and Malassezia.. At low concentrations terbinafine is fungicidal against dermatophytes, moulds and certain dimorphic fungi. The activity versus yeasts is fungicidal (Malassezia furfur [old name: Pityrosporum orbiculare]) or fungistatic depending on the species.

When given orally, the drug concentrates in skin, hair and nails at levels associated with fungicidal activity. It is still present there 15 to 20 days after stopping treatment.

Terbinafine is used for the treatment of fungal infections of the skin and nails, which is caused by Trichophyton (e.g. T. rubrum, T. mentagrophytes, T. verrucosum, T. violaceum), Microsporum canis and Epidermophyton floccosum. The following table outlines the range of minimum inhibitory concentrations (MIC) against the dermatophytes.

Organism	**MIC range (microgram/ml)**
Trichophyton rubrum	0.001 – 0.15
Trichophyton mentagrophytes	0.0001 – 0.05
Trichophyton verrucosum	0.001 – 0.006
Trichophyton violaceum	0.001 – 0.1
Microsporum canis	0.0001 – 0.1
Edidermorphyton fluccosum	0.001 – 0.05

Terbinafine exhibits poor efficacy against many yeasts of the Candida species and Malassezia.

Terbinafine tablets in contrast to locally administered terbinafine treatment, has no effect in the treatment of Pityriasis (Tinea) versicolor.

The enzyme squalene epoxidase is not linked to the cytochrome P450 system.

Clinical efficacy and safety

Onychomycosis

The efficacy of terbinafine tablets in the treatment of onychomycosis is illustrated by the response of patients with toenail and/or fingernail infections who participated in three US/Canadian placebo-controlled clinical trials (SFD301, SF5 and SF1508).

Results of the first toenail study, as assessed at week 48 (12 weeks of treatment with 36 weeks follow-up after completion of therapy), demonstrated mycological cure, defined as simultaneous occurrence of negative KOH plus negative culture, in 70% of patients. Fifty-nine percent (59%) of patients experienced effective treatment (mycological cure plus 0% nail involvement or > 5mm of new unaffected nail growth); 38% of patients demonstrated mycological cure plus clinical cure (0% nail involvement).

In a second toenail study of dermatophytic onychomycosis, in which non-dermatophytes were also cultured, similar efficacy against the dermatophytes was demonstrated. The pathogenic role of the non-dermatophytes cultured in the presence of dermatophytic onychomycosis has not been established. The clinical significance of this association is unknown.

Results of the fingernail study, as assessed at week 24 (6 weeks of treatment with 18 weeks follow-up after completion of therapy), demonstrated mycological cure in 79% of patients, effective treatment in 75% of the patients, and mycological cure plus clinical cure in 59% of the patients.

The mean time to treatment success for onychomycosis was approximately 10 months for the first toenail study and 4 months for the fingernail study. In the first toenail study, for patients evaluated at least six months after achieving clinical cure and at least one year after completing terbinafine therapy, the clinical relapse rate was approximately 15%.

Fungal infections of the skin (tinea corporis, tinea cruris,tinea pedis) and yeast infections of the skin caused by the genus Candida (e.g. Candida albicans) where oral therapy is generally considered appropriate owing to the site, severity or extent of the infection

Tinea corporis, tinea cruris

Three controlled, double blind, randomised, multicenter studies, 5OR (4 week study), 6-7OR (4 week study) and 11-21OR (6 week study), evaluated efficacy and safety of terbinafine tablets in the treatment of Tinea corporis and cruris.

Two double blind, placebo controlled studies (5OR, 6-7OR) evaluated the efficacy of terbinafine 125 mg b.i.d. in patients diagnosed with Tinea corporis/cruris. The studies included a total of 46 patients randomised to terbinafine and 49 on placebo. There was no significant difference in terms of demographic and anamnestic data within groups. Efficacy, demonstrated by negative mycology tests and a reduction in clinical symptomatology, was evaluated at 4 weeks and at the follow-up examination. As mycology tests, direct microscopy (presence of fungal mycelium in native preparation) and cultivation of mycelium from the native preparation (presence of fungal growth) were used. In both studies, minimal efficacy was demonstrated in patients treated with placebo compared to the efficacy of orally administered terbinafine at the end of therapy and at follow up. In the study 5OR a mycological cure and a reduction in clinical symptomatologywas achieved at the end of therapy in 73% and 54%, respectively, of patients treated with terbinafine 125 mg b.i.d.and in 89% and 62 %, respectively at follow up, compared to each 0% in placebo-treated patients.

In the study 6-7OR a mycological cure and a reduction in clinical symptomatology was achieved in 97% and 89%, respectively, of patients treated with terbinafine 125 mg b.i.d. at the end of therapy, compared with 29% and 12 %, respectively, of placebo treated patients. At follow up, a mycological cure and a reduction in clinical symptomatologywere achieved in 97% and 91%, respectively, of patients treated with terbinafine 125 mg b.i.d., compared with 37% and 21% of placebo-treated patients.

The third study (11-21OR), a 6 weeks, double blind, randomised, multicenter study compared efficacy and safety of terbinafine 125 mg b.i.d. to griseofulvin 250 mg b.i.d. One hundred twenty six (126) patients in each group were included in the efficacy analysis. This study showed for terbinafine 125 mg b.i.d. high rate of mycological cure (97% and 100%, respectively, of patients at the end of therapy and at follow up, compared with 90% and 94%, respectively, of patients treated with griseofulvin) and a significantly greater reduction in signs and symptoms in the terbinafine treated study arm at the end of therapy(93%) and at follow up (94%) compared with the comparator (86 and 87%, respectively).

Tinea pedis

Two double blind, controlled studies compared terbinafine 125 mg b.i.d. to placebo (39-40OR) and to griseofulvin 250 mg b.i.d. (20OR) in the treatment of Tinea pedis. Both studies recruited patients with chronic, recurrent disease. In the study 39-40OR, 65% of patients on terbinafine reported mycological cure at follow up whereas none of the placebo treated patients responded. In the study 20OR, terbinafine was shown to be highly effective with 88% of cure at follow up after 6 weeks therapy compared to 45% of patients on griseofulvin. These patients when observed after 10 months reported 94% cure rate, compared to 30% efficacy of griseofulvin in the same patient population.

5.2 Pharmacokinetic properties

Absorption
Fol lowin g ora l ad mi nis trati on, terbi nafi ne i s wel l ab sorb ed (>70 %). A single dose of 250 mg terbinafine resulted in m ean peak plasma concentrations of 1.3 microgram/m L with in 1 .5 ho urs of administration. At steady-state (70% steady state is achieved in approximately 28 days), in comparison to a single dose, peak concentration of terbinafine was on average 25% higher and plasma AUC increased by a factor of 2.3. From the increase in plasma AUC an effective half-life of approximately 30 hours can be calculated. The bioavailability of terbinafine is mod erate ly affected by food (in c rea s e in th e AUC of l es s th an 2 0%), but n ot s uffi cie ntly to requi re d ose adj ustm en ts.

Distribution
Terbinafine binds strongly to plasma proteins (99%). It rapidly diffuses through the skin and accumulates in the lipophilic stratum corneum. Terbinafine is also secreted in sebum, thus achieving high concentrations in hair follicles, hair and parts of the skin rich in sebaceous glands. There is also evidence that terbinafine is distributed into the nail plate in a few weeks after commencing therapy.

Biotransformation
Terbinafine is metabolised rapidly and extensively by at least seven CYP isoenzymes. It is mostly affected by CYP2C9, CYP1A2, CYP3A4, CYP2C8 and CYP2C19.

Elimination
Biotransformation produces metabolites which possess no antimycotic activity and which are predominantly excreted in the urine. Multiple dose administration followed by extended blood sampling revealed a triphasic elimination with a terminal half life of approximately 16.5 days.

Bioavailability
The absolute bioavailability of terbinafine from terbinafine tablets as a result of first-pass metabolism is approximately 50%.

Special populations
No c lin ica lly -rel eva nt age-dependent changes in steady state plasma concentrations of terbinafine have been observed, but the elimination may be slower in patients with renal or hepatic impairment.

Single dose pharmacokinetic studies in patients with renal impairment (creatinine clearance <50 ml/min) or with pre-existing mild to severe hepatic impairment have shown that the clearance of terbinafine can be reduced by about 50%.

5.3 Preclinical safety data

In longterm studies (up to 1 year) in rats and dogs no marked toxic effects were seen in either species up to oral doses of about 100 mg/kg a day. At high oral doses, the liver and possibly also the kidneys were identified as potential target organs.

In a two-year oral carcinogenicity study in mice, no neoplastic or other abnormal findings attributable to treatment were made up to doses of 130 (males) and 156 (females) mg/kg a day. In a two-year oral carcinogenicity study in rats, an increased incidence of liver tumours was observed in males at the highest dose level of 69 mg/kg a day, at which systemic exposure was similar to clinical exposure. The mechanism of tumour development has not been established. The clinical relevance is unknown. The changes, which might be associated with peroxisome proliferation, have been shown to be species-specific since they were not seen in the carcinogenicity study in mice, dogs or monkeys.

During high dose studies in monkeys, refractile irregularities were observed in the retina at the higher doses (non-toxic effect level 50 mg/kg). These irregularities were associated with the presence of a terbinafine metabolite in ocular tissue and disappeared after drug discontinuation. They were not associated with histological changes.

A standard battery of *in vitro* and in vivo genotoxicity tests revealed no evidence of mutagenic or clastogenic potential.

No adverse effects on fertility or other reproduction parameters were observed in studies in rats or rabbits.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Starch Glycolate (Type A)
Hypromellose
Silica, colloidal anhydrous
Potato starch
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Tablet container: Store in the original package in order to protect from light.
Blister: Keep the blisters in the outer carton in order to protect from light.

6.5 Nature and contents of container

Blister (Al/PVC) or polyethylene (HDPE) tablet containers and closures (tamper evident).

Pack sizes:
8, 10, 14, 20, 28, 30, 42, 56, 98 and 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

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

7 MARKETING AUTHORISATION HOLDER

Rowex Ltd
Newtown
Bantry
Co. Cork
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0711/071/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 11 March 2005
Date of last renewal: 16th June 2009

10 DATE OF REVISION OF THE TEXT

November 2019