ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Emselex 7.5 mg prolonged-release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 7.5 mg of darifenacin (as hydrobromide)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Prolonged-release tablet

White round, convex tablet, debossed with “DF” on one side and “7.5” on the reverse.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in adult patients with overactive bladder syndrome.

4.2 Posology and method of administration

Posology

Adults
The recommended starting dose is 7.5 mg daily. After 2 weeks of starting therapy, patients should be reassessed. For those patients requiring greater symptom relief, the dose may be increased to 15 mg daily, based on individual response.

Elderly patients (≥ 65 years)
The recommended starting dose for the elderly is 7.5 mg daily. After 2 weeks of starting therapy, patients should be reassessed for efficacy and safety. For those patients who have an acceptable tolerability profile but require greater symptom relief, the dose may be increased to 15 mg daily, based on individual response (see section 5.2).

Paediatric population
Emselex is not recommended for use in children below 18 years of age due to a lack of data on safety and efficacy.

Renal impairment
No dose adjustment is required in patients with impaired renal function. However, caution should be exercised when treating this population (see section 5.2).

Hepatic impairment
No dose adjustment is required in patients with mild hepatic impairment (Child Pugh A). However, there is a risk of increased exposure in this population (see section 5.2).

Patients with moderate hepatic impairment (Child Pugh B) should only be treated if the benefit outweighs the risk, and the dose should be restricted to 7.5 mg daily (see section 5.2). Emselex is contraindicated in patients with severe hepatic impairment (Child Pugh C) (see section 4.3).

Patients receiving concomitant treatment with substances that are potent inhibitors of CYP2D6 or moderate inhibitors of CYP3A4
In patients receiving substances that are potent CYP2D6 inhibitors, such as paroxetine, terbinafine, quinidine and cimetidine, treatment should start with the 7.5 mg dose. The dose may be titrated to 15 mg daily to obtain an improved clinical response provided the dose is well tolerated. However, caution should be exercised.

In patients receiving substances that are moderate CYP3A4 inhibitors, such as fluconazole, grapefruit juice and erythromycin, the recommended starting dose is 7.5 mg daily. The dose may be titrated to 15 mg daily to obtain an improved clinical response provided the dose is well tolerated. However, caution should be exercised.

Method of administration
Emselex is for oral use. The tablets should be taken once daily with liquid. They can be taken with or without food, and must be swallowed whole and not chewed, divided or crushed.

4.3 Contraindications

Emselex is contraindicated in patients with:
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Urinary retention.
- Gastric retention.
- Uncontrolled narrow-angle glaucoma.
- Myasthenia gravis.
- Severe hepatic impairment (Child Pugh C).
- Severe ulcerative colitis.
- Toxic megacolon.
- Concomitant treatment with potent CYP3A4 inhibitors (see section 4.5).

4.4 Special warnings and precautions for use

Emselex should be administered with caution to patients with autonomic neuropathy, hiatus hernia, clinically significant bladder outflow obstruction, risk for urinary retention, severe constipation or gastrointestinal obstructive disorders, such as pyloric stenosis.

Emselex should be used with caution in patients being treated for narrow-angle glaucoma (see section 4.3).

Other causes of frequent urination (heart failure or renal disease) should be assessed before treatment with Emselex. If urinary tract infection is present, an appropriate antibacterial therapy should be started.

Emselex should be used with caution in patients with risk of decreased gastrointestinal motility, gastro-oesophageal reflux and/or who are concurrently taking medicinal products (such as oral bisphosphonates) that can cause or exacerbate oesophagitis.

Safety and efficacy have not yet been established in patients with a neurogenic cause for detrusor over activity.

Caution should be used when prescribing antimuscarinics to patients with pre-existing cardiac diseases.

As with other antimuscarinics, patients should be instructed to discontinue Emselex and seek immediate medical attention if they experience oedema of the tongue or laropharynx, or difficulty breathing (see section 4.8).

4.5 Interaction with other medicinal products and other forms of interaction

Effects of other medicinal products on darifenacin
Darifenacin metabolism is primarily mediated by the cytochrome P450 enzymes CYP2D6 and CYP3A4. Therefore, inhibitors of these enzymes may increase darifenacin exposure.

CYP2D6 inhibitors
In patients receiving substances that are potent CYP2D6 inhibitors (e.g. paroxetine, terbinafine, cimetidine and quinidine) the recommended starting dose should be 7.5 mg daily. The dose may be titrated to 15 mg daily to obtain an improved clinical response provided the dose is well tolerated. Concomitant treatment with potent CYP2D6 inhibitors results in an increase in exposure (e.g. of 33% with 20 mg paroxetine at the 30 mg dose of darifenacin).

CYP3A4 inhibitors
Darifenacin should not be used together with potent CYP3A4 inhibitors (see section 4.3) such as protease inhibitors (e.g. ritonavir), ketoconazole and itraconazole. Potent P-glycoprotein inhibitors such as ciclosporin and verapamil should also be avoided. Co-administration of darifenacin 7.5 mg with the potent CYP3A4 inhibitor ketoconazole 400 mg resulted in a 5-fold increase in steady-state darifenacin AUC. In subjects who are poor metabolisers, darifenacin exposure increased approximately 10-fold. Due to a greater contribution of CYP3A4 after higher darifenacin doses, the magnitude of the effect is expected to be even more pronounced when combining ketoconazole with darifenacin 15 mg.

When co-administered with moderate CYP3A4 inhibitors such as erythromycin, clarithromycin, telithromycin, fluconazole and grapefruit juice, the recommended starting dose of darifenacin should be 7.5 mg daily. The dose may be titrated to 15 mg daily to obtain an improved clinical response provided the dose is well tolerated. Darifenacin AUC_{24} and C_{max} from 30 mg once daily dosing in subjects who are extensive metabolisers were 95% and 128% higher when erythromycin (moderate CYP3A4 inhibitor) was co-administered with darifenacin than when darifenacin was taken alone.

Enzyme inducers
Substances that are inducers of CYP3A4, such as rifampicin, carbamazepine, barbiturates and St John's wort (*Hypericum perforatum*) are likely to decrease the plasma concentrations of darifenacin.

Effects of darifenacin on other medicinal products
CYP2D6 substrates
Darifenacin is a moderate inhibitor of the enzyme CYP2D6. Caution should be exercised when darifenacin is used concomitantly with medicinal products that are predominantly metabolised by CYP2D6 and which have a narrow therapeutic window, such as flecainide, thioridazine, or tricyclic antidepressants such as imipramine. The effects of darifenacin on the metabolism of CYP2D6 substrates are mainly clinically relevant for CYP2D6 substrates which are individually dose titrated.

CYP3A4 substrates
Darifenacin treatment resulted in a modest increase in the exposure of the CYP3A4 substrate midazolam. However the data available do not indicate that darifenacin changes either midazolam clearance or bioavailability. It can therefore be concluded that darifenacin administration does not alter the pharmacokinetics of CYP3A4 substrates *in vivo*. The interaction with midazolam lacks clinical relevance, and therefore no dose adjustment is needed for CYP3A4 substrates.

Warfarin
Standard therapeutic prothrombin time monitoring for warfarin should be continued. The effect of warfarin on prothrombin time was not altered when co-administered with darifenacin.

Digoxin
Therapeutic drug monitoring for digoxin should be performed when initiating and ending darifenacin treatment as well as changing the darifenacin dose. Darifenacin 30 mg once daily (two times greater than the recommended daily dose) co-administered with digoxin at steady state resulted in a small

increase in digoxin exposure (AUC: 16% and C_{max}: 20%). The increase in digoxin exposure could be caused by competition between darifenacin and digoxin for P-glycoprotein. Other transporter-related interactions cannot be excluded.

Antimuscarinic agents
As with any other antimuscarinic agents, concomitant use of medicinal products that possess antimuscarinic properties, such as oxybutynin, tolterodine and flavoxate, may result in more pronounced therapeutic and side effects. The potentiation of anticholinergic effects with anti-parkinson agents and tricyclic antidepressants may also occur if antimuscarinic agents are used concurrently with such medicinal products. However, no studies involving the interaction with anti-parkinson agents and tricyclic antidepressants have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are limited amount of data from the use of darifenacin in pregnant women. Studies in animals have shown toxicity to parturition (for details, see section 5.3). Emselex is not recommended during pregnancy.

Breast-feeding
Darifenacin is excreted in the milk of rats. It is not known whether darifenacin is excreted in human milk. A risk to the nursing child cannot be excluded. A decision whether to avoid breast-feeding or to abstain from Emselex therapy during lactation should be based on a benefit and risk comparison.

Fertility
There are no human fertility data for darifenacin. Darifenacin had no effect on male or female fertility in rats or any effect in the reproductive organs of either sex in rats and dogs (for details, see section 5.3). Women of child bearing potential should be made aware of the lack of fertility data, and Emselex should only be given after consideration of individual risks and benefits.

4.7 Effects on ability to drive and use machines

As with other antimuscarinic agents, Emselex may produce effects such as dizziness, blurred vision, insomnia and somnolence. Patients experiencing these side effects should not drive or use machines. For Emselex, these side effects have been reported to be uncommon.

4.8 Undesirable effects

Summary of the safety profile
Consistent with the pharmacological profile, the most commonly reported adverse reactions were dry mouth (20.2% and 35% for the 7.5 mg and 15 mg dose, respectively, 18.7% after flexible dose titration, and 8% - 9% for placebo) and constipation (14.8% and 21% for the 7.5 mg and 15 mg dose, respectively, 20.9% after flexible dose titration, and 5.4% - 7.9% for placebo). Anticholinergic effects, in general, are dose-dependent.

However, the patient discontinuation rates due to these adverse reactions were low (dry mouth: 0% - 0.9% and constipation: 0.6% - 2.2% for darifenacin, depending on the dose; and 0% and 0.3% for placebo, for dry mouth and constipation, respectively).

Tabulated list of adverse reactions
The adverse reactions are ranked under heading of frequency using 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) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: Adverse reactions with Emselex 7.5 mg and 15 mg prolonged-release tablets

Infections and infestations	
Uncommon	Urinary tract infection
Psychiatric disorders	
Uncommon	Insomnia, thinking abnormal
Nervous system disorders	
Common Uncommon	Headache Dizziness, dysgeusia, somnolence
Eye disorders	
Common Uncommon	Dry eye Visual disturbance, including vision blurred
Vascular disorders	
Uncommon	Hypertension
Respiratory, thoracic and mediastinal disorders	
Common Uncommon	Nasal dryness Dyspnoea, cough, rhinitis
Gastrointestinal disorders	
Very common Common Uncommon	Constipation, dry mouth Abdominal pain, nausea, dyspepsia Flatulence, diarrhoea, mouth ulceration
Skin and subcutaneous tissue disorders	
Uncommon Not known	Rash, dry skin, pruritus, hyperhidrosis Angioedema
Renal and urinary disorders	
Uncommon	Urinary retention, urinary tract disorder, bladder pain
Reproductive system and breast disorders	
Uncommon	Erectile dysfunction, vaginitis
General disorders and administration site conditions	
Uncommon	Oedema peripheral, asthenia, face oedema, oedema
Investigations	
Uncommon	Aspartate aminotransferase increased, alanine aminotransferase increased
Injury, poisoning, and procedural complications	
Uncommon	Injury

Description of selected adverse reactions

In the pivotal clinical trials with doses of Emselex 7.5 mg and 15 mg, adverse reactions were reported as presented in the table above. Most of the adverse reactions were of mild or moderate intensity and did not result in discontinuation in the majority of the patients.

Treatment with Emselex may possibly mask symptoms associated with gallbladder disease. However, there was no association between the occurrence of adverse events related to the biliary system in darifenacin-treated patients and increasing age.

The incidence of adverse reactions with the doses of Emselex 7.5 mg and 15 mg decreased during the treatment period up to 6 months. A similar trend is also seen for the discontinuation rates.

Post-marketing experience

The following events have been reported in association with darifenacin use in worldwide post-marketing experience: generalised hypersensitivity reactions including angioedema, depressed mood/mood alterations, hallucination. Because these spontaneously reported events are from the worldwide post-marketing experience, the frequency of events cannot be estimated from the available data.

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 the national reporting system listed in Appendix V.

4.9 Overdose

Emselex has been administered in clinical trials at doses up to 75 mg (five times maximum therapeutic dose). The most common adverse reactions seen were dry mouth, constipation, headache, dyspepsia and nasal dryness. However, overdose with darifenacin can potentially lead to severe anticholinergic effects and should be treated accordingly. Therapy should be aimed at reversing the anticholinergic symptoms under careful medical supervision. The use of agents such as physostigmine can assist in reversing such symptoms.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals, drugs for urinary frequency and incontinence; ATC code: G04BD10.

Mechanism of action
Darifenacin is a selective muscarinic M3 receptor antagonist (M_3 SRA) *in vitro*. The M3 receptor is the major subtype that controls urinary bladder muscle contraction. It is not known whether this selectivity for the M3 receptor translates into any clinical advantage when treating symptoms of overactive bladder syndrome.

Clinical efficacy and safety
Cystometric studies performed with darifenacin in patients with involuntary bladder contractions showed increased bladder capacity, increased volume threshold for unstable contractions and diminished frequency of unstable detrusor contractions.

Treatment with Emselex administered at dosages of 7.5 mg and 15 mg daily has been investigated in four double-blind, Phase III, randomised, controlled clinical studies in male and female patients with symptoms of overactive bladder. As seen in Table 2 below, a pooled analysis of 3 of the studies for the treatment with both Emselex 7.5 mg and 15 mg provided a statistically significant improvement in the primary endpoint, reduction in incontinence episodes, versus placebo.

Table 2: Pooled analysis of data from three Phase III clinical studies assessing fixed doses of 7.5 mg and 15 mg Emselex

Dose	N	Incontinence episodes per week				95% CI	P value[2]
		Baseline (median)	Week 12 (median)	Change from baseline (median)	Differences from placebo[1] (median)		
Emselex 7.5 mg once daily	335	16.0	4.9	-8.8 (-68%)	-2.0	(-3.6, -0.7)	0.004
Placebo	271	16.6	7.9	-7.0 (-54%)	--	--	--
Emselex 15 mg once daily	330	16.9	4.1	-10.6 (-77%)	-3.2	(-4.5, -2.0)	<0.001
Placebo	384	16.6	6.4	-7.5 (-58%)	--	--	--

[1] Hodges Lehmann estimate: median difference from placebo in change from baseline
[2] Stratified Wilcoxon test for difference from placebo.

Emselex 7.5 mg and 15 mg doses significantly reduced both the severity and number of urinary urgency episodes and the number of micturitions, while significantly increasing the mean volume voided from baseline.

Emselex 7.5 mg and 15 mg were associated with statistically significant improvements over placebo in some aspects of quality of life as measured by the Kings Health Questionnaire including incontinence impact, role limitations, social limitations and severity measures.

For both doses of 7.5 mg and 15 mg, the percentage median reduction from baseline in the number of incontinence episodes per week was similar between males and females. The observed differences from placebo for males in terms of percentage and absolute reductions in incontinence episodes was lower than for females.

The effect of treatment with 15 mg and 75 mg of darifenacin on QT/QTc interval was evaluated in a study in 179 healthy adults (44% male: 56% females) aged 18 to 65 for 6 days (to steady state). Therapeutic and supra-therapeutic doses of darifenacin resulted in no increase in QT/QTc interval prolongation from baseline compared to placebo at maximum darifenacin exposure.

5.2 Pharmacokinetic properties

Darifenacin is metabolised by CYP3A4 and CYP2D6. Due to genetic differences, about 7% of the Caucasians lack the CYP2D6 enzyme and are said to be poor metabolisers. A few percent of the population have increased CYP2D6 enzyme levels (ultrafast metabolisers). The information below applies to subjects who have normal CYP2D6 activity (extensive metabolisers) unless otherwise stated.

Absorption
Due to extensive first-pass metabolism darifenacin has a bioavailability of approximately 15% and 19% after 7.5 mg and 15 mg daily doses at steady state. Maximum plasma levels are reached approximately 7 hours after administration of the prolonged-release tablets and steady-state plasma levels are achieved by the sixth day of administration. At steady state, peak-to-trough fluctuations in darifenacin concentrations are small (PTF: 0.87 for 7.5 mg and 0.76 for 15 mg), thereby maintaining therapeutic plasma levels over the dosing interval. Food had no effect on darifenacin pharmacokinetics during multiple-dose administration of prolonged-release tablets.

Distribution
Darifenacin is a lipophilic base and is 98% bound to plasma proteins (primarily to alpha-1-acid-glycoprotein). The steady-state volume of distribution (V_{ss}) is estimated to be 163 litres.

Metabolism
Darifenacin is extensively metabolised by the liver following oral administration.

Darifenacin undergoes significant metabolism by cytochrome CYP3A4 and CYP2D6 in the liver and by CYP3A4 in the gut wall. The three main metabolic routes are as follows:
monohydroxylation in the dihydrobenzofuran ring;
dihydrobenzofuran ring opening and
N-dealkylation of the pyrrolidine nitrogen.

The initial products of the hydroxylation and N-dealkylation pathways are major circulating metabolites but none contribute significantly to the overall clinical effect of darifenacin.

The pharmacokinetics of darifenacin at steady state are dose-dependent, due to saturation of the CYP2D6 enzyme.

Doubling the darifenacin dose from 7.5 mg to 15 mg result in a 150% increase in steady-state exposure. This dose-dependency is probably caused by saturation of the CYP2D6 catalysed metabolism possibly together with some saturation of CYP3A4-mediated gut wall metabolism.

Excretion
Following administration of an oral dose of ^{14}C-darifenacin solution to healthy volunteers, approximately 60% of the radioactivity was recovered in the urine and 40% in the faeces. Only a small percentage of the excreted dose was unchanged darifenacin (3%). Estimated darifenacin clearance is 40 litres/hour. The elimination half-life of darifenacin following chronic dosing is approximately 13-19 hours.

Special patient population
Gender
A population pharmacokinetic analysis of patient data indicated that darifenacin exposure was 23% lower in males than females (see section 5.1).

Elderly patients
A population pharmacokinetic analysis of patient data indicated a trend for clearance to decrease with age (19% per decade based on Phase III population pharmacokinetic analysis of patients aged 60–89 years), see section 4.2.

Paediatric patients
The pharmacokinetics of darifenacin have not been established in the paediatric population.

CYP2D6 poor metabolisers
The metabolism of darifenacin in CYP2D6 poor metabolisers is principally mediated by CYP3A4. In one pharmacokinetic study the steady-state exposure in poor metabolisers was 164% and 99% higher during treatment with 7.5 mg and 15 mg once daily, respectively. However, a population pharmacokinetic analyses of Phase III data indicated that on average steady-state exposure is 66% higher in poor metabolisers than in extensive metabolisers. There was considerable overlap between the ranges of exposures seen in these two populations (see section 4.2).

Renal insufficiency
A small study of subjects (n=24) with varying degrees of renal impairment (creatinine clearance between 10 ml/min and 136 ml/min) given darifenacin 15 mg once daily to steady state demonstrated no relationship between renal function and darifenacin clearance (see section 4.2).

Hepatic insufficiency
Darifenacin pharmacokinetics were investigated in subjects with mild (Child Pugh A) or moderate (Child Pugh B) impairment of hepatic function given darifenacin 15 mg once daily to steady state. Mild hepatic impairment had no effect on the pharmacokinetics of darifenacin. However, protein binding of darifenacin was affected by moderate hepatic impairment. Unbound darifenacin exposure was estimated to be 4.7-fold higher in subjects with moderate hepatic impairment than subjects with normal hepatic function (see section 4.2).

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. There were no effects on fertility in male and female rats treated at oral doses up to 50 mg/kg/day (78 times the $AUC_{0\text{-}24h}$ of free plasma concentration at maximum recommended human dose [MRHD]). There were no effects on reproductive organs in either sex in dogs treated for 1 year at oral doses up to 6 mg/kg/day (82 times the $AUC_{0\text{-}24h}$ of free plasma concentration at MRHD). Darifenacin was not teratogenic in rats and rabbits at doses up to 50 and 30 mg/kg/day, respectively. At the dose of 50 mg/kg/day in rats (59 times the $AUC_{0\text{-}24h}$ of free plasma concentration at MRHD), delay in the ossification of the sacral and caudal vertebrae was observed. At the dose of 30 mg/kg/day in rabbits (28 times the $AUC_{0\text{-}24h}$ of free plasma concentration at MRHD), maternal toxicity and foetotoxicity (increased post implantation loss and decreased number of viable foetuses per litter) were observed. In peri and post-natal studies in rats, dystocia, increased foetal deaths *in utero* and toxicity to post-natal development (pup body weight

and development land marks) were observed at systemic exposure levels up to 11 times the AUC_{0-24h} of free plasma concentration at MRHD.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Calcium hydrogen phosphate, anhydrous
Hypromellose
Magnesium stearate

Film coat
Polyethylene glycol
Hypromellose
Titanium dioxide (E171)
Talc

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Keep the blister packs in the outer carton in order to protect from light.

6.5 Nature and contents of container

Clear PVC/CTFE/aluminium or PVC/PVDC/aluminium blisters in cartons containing 7, 14, 28, 49, 56 or 98 tablets as unit pack or in multipacks containing 140 (10x14) tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

pharmaand GmbH
Taborstrasse 1
1020 Vienna
Austria

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/294/001-006
EU/1/04/294/013
EU/1/04/294/015-020
EU/1/04/294/027

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 October 2004
Date of latest renewal: 24 September 2009

10. DATE OF REVISION OF THE TEXT

Detailed information on this product is available on the website of the European Medicines Agency http://www.ema.europa.eu

1. NAME OF THE MEDICINAL PRODUCT

Emselex 15 mg prolonged-release tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 15 mg of darifenacin (as hydrobromide)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Prolonged-release tablet

Light peach round, convex tablet debossed with “DF” on one side and “15” on the reverse.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in adult patients with overactive bladder syndrome.

4.2 Posology and method of administration

Posology

Adults
The recommended starting dose is 7.5 mg daily. After 2 weeks of starting therapy, patients should be reassessed. For those patients requiring greater symptom relief, the dose may be increased to 15 mg daily, based on individual response.

Elderly patients (≥ 65 years)
The recommended starting dose for the elderly is 7.5 mg daily. After 2 weeks of starting therapy, patients should be reassessed for efficacy and safety. For those patients who have an acceptable tolerability profile but require greater symptom relief, the dose may be increased to 15 mg daily, based on individual response (see section 5.2).

Paediatric population
Emselex is not recommended for use in children below 18 years of age due to a lack of data on safety and efficacy.

Renal impairment
No dose adjustment is required in patients with impaired renal function. However, caution should be exercised when treating this population (see section 5.2).

Hepatic impairment
No dose adjustment is required in patients with mild hepatic impairment (Child Pugh A). However, there is a risk of increased exposure in this population (see section 5.2).

Patients with moderate hepatic impairment (Child Pugh B) should only be treated if the benefit outweighs the risk, and the dose should be restricted to 7.5 mg daily (see section 5.2). Emselex is contraindicated in patients with severe hepatic impairment (Child Pugh C) (see section 4.3).

Patients receiving concomitant treatment with substances that are potent inhibitors of CYP2D6 or moderate inhibitors of CYP3A4
In patients receiving substances that are potent CYP2D6 inhibitors, such as paroxetine, terbinafine, quinidine and cimetidine, treatment should start with the 7.5 mg dose. The dose may be titrated to 15 mg daily to obtain an improved clinical response provided the dose is well tolerated. However, caution should be exercised.

In patients receiving substances that are moderate CYP3A4 inhibitors, such as fluconazole, grapefruit juice and erythromycin, the recommended starting dose is 7.5 mg daily. The dose may be titrated to 15 mg daily to obtain an improved clinical response provided the dose is well tolerated. However, caution should be exercised.

Method of administration
Emselex is for oral use. The tablets should be taken once daily with liquid. They can be taken with or without food, and must be swallowed whole and not chewed, divided or crushed.

4.3 Contraindications

Emselex is contraindicated in patients with:
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Urinary retention.
- Gastric retention.
- Uncontrolled narrow-angle glaucoma.
- Myasthenia gravis.
- Severe hepatic impairment (Child Pugh C).
- Severe ulcerative colitis.
- Toxic megacolon.
- Concomitant treatment with potent CYP3A4 inhibitors (see section 4.5).

4.4 Special warnings and precautions for use

Emselex should be administered with caution to patients with autonomic neuropathy, hiatus hernia, clinically significant bladder outflow obstruction, risk for urinary retention, severe constipation or gastrointestinal obstructive disorders, such as pyloric stenosis.

Emselex should be used with caution in patients being treated for narrow-angle glaucoma (see section 4.3).

Other causes of frequent urination (heart failure or renal disease) should be assessed before treatment with Emselex. If urinary tract infection is present, an appropriate antibacterial therapy should be started.

Emselex should be used with caution in patients with risk of decreased gastrointestinal motility, gastro-oesophageal reflux and/or who are concurrently taking medicinal products (such as oral bisphosphonates) that can cause or exacerbate oesophagitis.

Safety and efficacy have not yet been established in patients with a neurogenic cause for detrusor over activity.

Caution should be used when prescribing antimuscarinics to patients with pre-existing cardiac diseases.

As with other antimuscarinics, patients should be instructed to discontinue Emselex and seek immediate medical attention if they experience oedema of the tongue or laropharynx, or difficulty breathing (see section 4.8).

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CYP3A4 inhibitors
Darifenacin should not be used together with potent CYP3A4 inhibitors (see section 4.3) such as protease inhibitors (e.g. ritonavir), ketoconazole and itraconazole. Potent P-glycoprotein inhibitors such as ciclosporin and verapamil should also be avoided. Co-administration of darifenacin 7.5 mg with the potent CYP3A4 inhibitor ketoconazole 400 mg resulted in a 5-fold increase in steady-state darifenacin AUC. In subjects who are poor metabolisers, darifenacin exposure increased approximately 10-fold. Due to a greater contribution of CYP3A4 after higher darifenacin doses, the magnitude of the effect is expected to be even more pronounced when combining ketoconazole with darifenacin 15 mg.

When co-administered with moderate CYP3A4 inhibitors such as erythromycin, clarithromycin, telithromycin, fluconazole and grapefruit juice, the recommended starting dose of darifenacin should be 7.5 mg daily. The dose may be titrated to 15 mg daily to obtain an improved clinical response provided the dose is well tolerated. Darifenacin AUC_{24} and C_{max} from 30 mg once-daily dosing in subjects who are extensive metabolisers were 95% and 128% higher when erythromycin (moderate CYP3A4 inhibitor) was co-administered with darifenacin than when darifenacin was taken alone.

Enzyme inducers
Substances that are inducers of CYP3A4, such as rifampicin, carbamazepine, barbiturates and St John´s wort (*Hypericum perforatum*) are likely to decrease the plasma concentrations of darifenacin.

Effects of darifenacin on other medicinal products
CYP2D6 substrates
Darifenacin is a moderate inhibitor of the enzyme CYP2D6. Caution should be exercised when darifenacin is used concomitantly with medicinal products that are predominantly metabolised by CYP2D6 and which have a narrow therapeutic window, such as flecainide, thioridazine, or tricyclic antidepressants such as imipramine. The effects of darifenacin on the metabolism of CYP2D6 substrates are mainly clinically relevant for CYP2D6 substrates which are individually dose titrated.

CYP3A4 substrates
Darifenacin treatment resulted in a modest increase in the exposure of the CYP3A4 substrate midazolam. However the data available do not indicate that darifenacin changes either midazolam clearance or bioavailability. It can therefore be concluded that darifenacin administration does not alter the pharmacokinetics of CYP3A4 substrates *in vivo*. The interaction with midazolam lacks clinical relevance, and therefore no dose adjustment is needed for CYP3A4 substrates.

Warfarin
Standard therapeutic prothrombin time monitoring for warfarin should be continued. The effect of warfarin on prothrombin time was not altered when co-administered with darifenacin.

Digoxin
Therapeutic drug monitoring for digoxin should be performed when initiating and ending darifenacin treatment as well as changing the darifenacin dose. Darifenacin 30 mg once daily (two times greater than the recommended daily dose) co-administered with digoxin at steady state resulted in a small

increase in digoxin exposure (AUC: 16% and C_{max}: 20%). The increase in digoxin exposure could be caused by competition between darifenacin and digoxin for P-glycoprotein. Other transporter-related interactions cannot be excluded.

Antimuscarinic agents
As with any other antimuscarinic agents, concomitant use of medicinal products that possess antimuscarinic properties, such as oxybutynin, tolterodine and flavoxate, may result in more pronounced therapeutic and side effects. The potentiation of anticholinergic effects with anti-parkinson agents and tricyclic antidepressants may also occur if antimuscarinic agents are used concurrently with such medicinal products. However, no studies involving the interaction with anti-parkinson agents and tricyclic antidepressants have been performed.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are limited amount of data from the use of darifenacin in pregnant women. Studies in animals have shown toxicity to parturition (for details, see section 5.3). Emselex is not recommended during pregnancy.

Breast-feeding
Darifenacin is excreted in the milk of rats. It is not known whether darifenacin is excreted in human milk. A risk to the nursing child cannot be excluded. A decision whether to avoid breast-feeding or to abstain from Emselex therapy during lactation should be based on a benefit and risk comparison.

Fertility
There are no human fertility data for darifenacin. Darifenacin had no effect on male or female fertility in rats or any effect in the reproductive organs of either sex in rats and dogs (for details, see section 5.3). Women of child bearing potential should be made aware of the lack of fertility data, and Emselex should only be given after consideration of individual risks and benefits.

4.7 Effects on ability to drive and use machines

As with other antimuscarinic agents, Emselex may produce effects such as dizziness, blurred vision, insomnia and somnolence. Patients experiencing these side effects should not drive or use machines. For Emselex, these side effects have been reported to be uncommon.

4.8 Undesirable effects

Summary of the safety profile
Consistent with the pharmacological profile, the most commonly reported adverse reactions were dry mouth (20.2% and 35% for the 7.5 mg and 15 mg dose, respectively, 18.7% after flexible dose titration, and 8% - 9% for placebo) and constipation (14.8% and 21% for the 7.5 mg and 15 mg dose, respectively, 20.9% after flexible dose titration, and 5.4% - 7.9% for placebo). Anticholinergic effects, in general, are dose-dependent.

However, the patient discontinuation rates due to these adverse reactions were low (dry mouth: 0% - 0.9% and constipation: 0.6% - 2.2% for darifenacin, depending on the dose; and 0% and 0.3% for placebo, for dry mouth and constipation, respectively).

Tabulated list of adverse reactions
The adverse reactions are ranked under heading of frequency using 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) and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1: Adverse reactions with Emselex 7.5 mg and 15 mg prolonged-release tablets

Infections and infestations	
Uncommon	Urinary tract infection
Psychiatric disorders	
Uncommon	Insomnia, thinking abnormal
Nervous system disorders	
Common Uncommon	Headache Dizziness, dysgeusia, somnolence
Eye disorders	
Common Uncommon	Dry eye Visual disturbance, including vision blurred
Vascular disorders	
Uncommon	Hypertension
Respiratory, thoracic and mediastinal disorders	
Common Uncommon	Nasal dryness Dyspnoea, cough, rhinitis
Gastrointestinal disorders	
Very common Common Uncommon	Constipation, dry mouth Abdominal pain, nausea, dyspepsia Flatulence, diarrhoea, mouth ulceration
Skin and subcutaneous tissue disorders	
Uncommon Not known	Rash, dry skin, pruritus, hyperhidrosis Angioedema
Renal and urinary disorders	
Uncommon	Urinary retention, urinary tract disorder, bladder pain
Reproductive system and breast disorders	
Uncommon	Erectile dysfunction, vaginitis
General disorders and administration site conditions	
Uncommon	Oedema peripheral, asthenia, face oedema, oedema
Investigations	
Uncommon	Aspartate aminotransferase increased, alanine aminotransferase increased
Injury, poisoning, and procedural complications	
Uncommon	Injury

Description of selected adverse reactions

In the pivotal clinical trials with doses of Emselex 7.5 mg and 15 mg, adverse reactions were reported as presented in the table above. Most of the adverse reactions were of mild or moderate intensity and did not result in discontinuation in the majority of the patients.

Treatment with Emselex may possibly mask symptoms associated with gallbladder disease. However, there was no association between the occurrence of adverse events related to the biliary system in darifenacin-treated patients and increasing age.

The incidence of adverse reactions with the doses of Emselex 7.5 mg and 15 mg decreased during the treatment period up to 6 months. A similar trend is also seen for the discontinuation rates.

Post-marketing experience

The following events have been reported in association with darifenacin use in worldwide post-marketing experience: generalised hypersensitivity reactions including angioedema, depressed mood/mood alterations, hallucination. Because these spontaneously reported events are from the worldwide post-marketing experience, the frequency of events cannot be estimated from the available data.

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 the national reporting system listed in Appendix V.

4.9 Overdose

Emselex has been administered in clinical trials at doses up to 75 mg (five times maximum therapeutic dose). The most common adverse reactions seen were dry mouth, constipation, headache, dyspepsia and nasal dryness. However, overdose with darifenacin can potentially lead to severe anticholinergic effects and should be treated accordingly. Therapy should be aimed at reversing the anticholinergic symptoms under careful medical supervision. The use of agents such as physostigmine can assist in reversing such symptoms.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals, drugs for urinary frequency and incontinence; ATC code: G04BD10.

Mechanism of action
Darifenacin is a selective muscarinic M3 receptor antagonist (M_3 SRA) *in vitro*. The M3 receptor is the major subtype that controls urinary bladder muscle contraction. It is not known whether this selectivity for the M3 receptor translates into any clinical advantage when treating symptoms of overactive bladder syndrome.

Clinical efficacy and safety
Cystometric studies performed with darifenacin in patients with involuntary bladder contractions showed increased bladder capacity, increased volume threshold for unstable contractions and diminished frequency of unstable detrusor contractions.

Treatment with Emselex administered at dosages of 7.5 mg and 15 mg daily has been investigated in four double-blind, Phase III, randomised, controlled clinical studies in male and female patients with symptoms of overactive bladder. As seen in Table 2 below, a pooled analysis of 3 of the studies for the treatment with both Emselex 7.5 mg and 15 mg provided a statistically significant improvement in the primary endpoint, reduction in incontinence episodes, versus placebo.

Table 2: Pooled analysis of data from three Phase III clinical studies assessing fixed doses of 7.5 mg and 15 mg Emselex

Dose	N	Incontinence episodes per week				95% CI	P value[2]
		Baseline (median)	Week 12 (median)	Change from baseline (median)	Differences from placebo[1] (median)		
Emselex 7.5 mg once daily	335	16.0	4.9	-8.8 (-68%)	-2.0	(-3.6, -0.7)	0.004
Placebo	271	16.6	7.9	-7.0 (-54%)	--	--	--
Emselex 15 mg once daily	330	16.9	4.1	-10.6 (-77%)	-3.2	(-4.5, -2.0)	<0.001
Placebo	384	16.6	6.4	-7.5 (-58%)	--	--	--

[1] Hodges Lehmann estimate: median difference from placebo in change from baseline
[2] Stratified Wilcoxon test for difference from placebo.

Emselex 7.5 mg and 15 mg doses significantly reduced both the severity and number of urinary urgency episodes and the number of micturitions, while significantly increasing the mean volume voided from baseline.

Emselex 7.5 mg and 15 mg were associated with statistically significant improvements over placebo in some aspects of quality of life as measured by the Kings Health Questionnaire including incontinence impact, role limitations, social limitations and severity measures.

For both doses of 7.5 mg and 15 mg, the percentage median reduction from baseline in the number of incontinence episodes per week was similar between males and females. The observed differences from placebo for males in terms of percentage and absolute reductions in incontinence episodes was lower than for females.

The effect of treatment with 15 mg and 75 mg of darifenacin on QT/QTc interval was evaluated in a study in 179 healthy adults (44% male: 56% females) aged 18 to 65 for 6 days (to steady state). Therapeutic and supra-therapeutic doses of darifenacin resulted in no increase in QT/QTc interval prolongation from baseline compared to placebo at maximum darifenacin exposure.

5.2 Pharmacokinetic properties

Darifenacin is metabolised by CYP3A4 and CYP2D6. Due to genetic differences, about 7% of the Caucasians lack the CYP2D6 enzyme and are said to be poor metabolisers. A few percent of the population have increased CYP2D6 enzyme levels (ultrafast metabolisers). The information below applies to subjects who have normal CYP2D6 activity (extensive metabolisers) unless otherwise stated.

Absorption
Due to extensive first-pass metabolism darifenacin has a bioavailability of approximately 15% and 19% after 7.5 mg and 15 mg daily doses at steady state. Maximum plasma levels are reached approximately 7 hours after administration of the prolonged-release tablets and steady-state plasma levels are achieved by the sixth day of administration. At steady state, peak-to-trough fluctuations in darifenacin concentrations are small (PTF: 0.87 for 7.5 mg and 0.76 for 15 mg), thereby maintaining therapeutic plasma levels over the dosing interval. Food had no effect on darifenacin pharmacokinetics during multiple-dose administration of prolonged-release tablets.

Distribution
Darifenacin is a lipophilic base and is 98% bound to plasma proteins (primarily to alpha-1-acid-glycoprotein). The steady-state volume of distribution (V_{ss}) is estimated to be 163 litres.

Metabolism

Darifenacin is extensively metabolised by the liver following oral administration.

Darifenacin undergoes significant metabolism by cytochrome CYP3A4 and CYP2D6 in the liver and by CYP3A4 in the gut wall. The three main metabolic routes are as follows:
monohydroxylation in the dihydrobenzofuran ring;
dihydrobenzofuran ring opening and
N-dealkylation of the pyrrolidine nitrogen.

The initial products of the hydroxylation and N-dealkylation pathways are major circulating metabolites but none contribute significantly to the overall clinical effect of darifenacin.

The pharmacokinetics of darifenacin at steady state are dose-dependent, due to saturation of the CYP2D6 enzyme.

Doubling the darifenacin dose from 7.5 mg to 15 mg result in a 150% increase in steady-state exposure. This dose-dependency is probably caused by saturation of the CYP2D6 catalysed metabolism possibly together with some saturation of CYP3A4-mediated gut wall metabolism.

Excretion
Following administration of an oral dose of ^{14}C-darifenacin solution to healthy volunteers, approximately 60% of the radioactivity was recovered in the urine and 40% in the faeces. Only a small percentage of the excreted dose was unchanged darifenacin (3%). Estimated darifenacin clearance is 40 litres/hour. The elimination half-life of darifenacin following chronic dosing is approximately 13-19 hours.

Special patient population
Gender
A population pharmacokinetic analysis of patient data indicated that darifenacin exposure was 23% lower in males than females (see section 5.1).

Elderly patients
A population pharmacokinetic analysis of patient data indicated a trend for clearance to decrease with age (19% per decade based on Phase III population pharmacokinetic analysis of patients aged 60–89 years), see section 4.2.

Paediatric patients
The pharmacokinetics of darifenacin have not been established in the paediatric population.

CYP2D6 poor metabolisers
The metabolism of darifenacin in CYP2D6 poor metabolisers is principally mediated by CYP3A4. In one pharmacokinetic study the steady-state exposure in poor metabolisers was 164% and 99% higher during treatment with 7.5 mg and 15 mg once daily, respectively. However, a population pharmacokinetic analyses of Phase III data indicated that on average steady-state exposure is 66% higher in poor metabolisers than in extensive metabolisers. There was considerable overlap between the ranges of exposures seen in these two populations (see section 4.2).

Renal insufficiency
A small study of subjects (n=24) with varying degrees of renal impairment (creatinine clearance between 10 ml/min and 136 ml/min) given darifenacin 15 mg once daily to steady state demonstrated no relationship between renal function and darifenacin clearance (see section 4.2).

Hepatic insufficiency
Darifenacin pharmacokinetics were investigated in subjects with mild (Child Pugh A) or moderate (Child Pugh B) impairment of hepatic function given darifenacin 15 mg once daily to steady state. Mild hepatic impairment had no effect on the pharmacokinetics of darifenacin. However, protein binding of darifenacin was affected by moderate hepatic impairment. Unbound darifenacin exposure

was estimated to be 4.7-fold higher in subjects with moderate hepatic impairment than subjects with normal hepatic function (see section 4.2).

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. There were no effects on fertility in male and female rats treated at oral doses up to 50 mg/kg/day (78 times the $AUC_{0\text{-}24h}$ of free plasma concentration at maximum recommended human dose [MRHD]). There were no effects on reproductive organs in either sex in dogs treated for 1 year at oral doses up to 6 mg/kg/day (82 times the $AUC_{0\text{-}24h}$ of free plasma concentration at MRHD). Darifenacin was not teratogenic in rats and rabbits at doses up to 50 and 30 mg/kg/day, respectively. At the dose of 50 mg/kg/day in rats (59 times the $AUC_{0\text{-}24h}$ of free plasma concentration at MRHD), delay in the ossification of the sacral and caudal vertebrae was observed. At the dose of 30 mg/kg/day in rabbits (28 times the $AUC_{0\text{-}24h}$ of free plasma concentration at MRHD), maternal toxicity and foetotoxicity (increased post implantation loss and decreased number of viable foetuses per litter) were observed. In peri and post-natal studies in rats, dystocia, increased foetal deaths *in utero* and toxicity to post-natal development (pup body weight and development land marks) were observed at systemic exposure levels up to 11 times the $AUC_{0\text{-}24h}$ of free plasma concentration at MRHD.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Calcium hydrogen phosphate, anhydrous
Hypromellose
Magnesium stearate

Film coat
Polyethylene glycol
Hypromellose
Talc
Titanium dioxide (E171)
Yellow iron oxide (E172)
Red iron oxide (E172)

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Keep the blister packs in the outer carton in order to protect from light.

6.5 Nature and contents of container

Clear PVC/CTFE/aluminium or PVC/PVDC/aluminium blisters in cartons containing 7, 14, 28, 49, 56 or 98 tablets as unit pack or in multipacks containing 140 (10x14) tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

pharmaand GmbH
Taborstrasse 1
1020 Vienna
Austria

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/294/007-012
EU/1/04/294/014
EU/1/04/294/021-026
EU/1/04/294/028

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 October 2004
Date of latest renewal: 24 September 2009

10. DATE OF REVISION OF THE TEXT

Detailed information on this product is available on the website of the European Medicines Agency http://www.ema.europa.eu

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

DREHM Pharma GmbH
Grünbergstrasse 15/3/3
1120 Vienna
Austria

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:
- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK

1. NAME OF THE MEDICINAL PRODUCT

Emselex 7.5 mg prolonged-release tablets
darifenacin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 7.5 mg darifenacin (as hydrobromide).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

7 tablets
14 tablets
28 tablets
49 tablets
56 tablets
98 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Keep the blister packs in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

pharmaand GmbH
Taborstrasse 1
1020 Vienna, Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/294/001	7 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/002	14 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/003	28 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/004	49 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/005	56 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/006	98 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/015	7 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/016	14 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/017	28 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/018	49 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/019	56 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/020	98 tablets (PVC/PVDC/alu blisters)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Emselex 7.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACKS (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Emselex 7.5 mg prolonged-release tablets
darifenacin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 7.5 mg darifenacin (as hydrobromide).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

140 tablets
Multipack comprising 10 packs, each containing 14 tablets.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Keep the blister packs in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

pharmaand GmbH
Taborstrasse 1
1020 Vienna, Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/294/013 (PVC/CTFE/alu blisters)
EU/1/04/294/027 (PVC/PVDC/alu blisters)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Emselex 7.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACKS (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Emselex 7.5 mg prolonged-release tablets
darifenacin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 7.5 mg darifenacin (as hydrobromide).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 tablets
Component of a multipack, not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Keep the blister packs in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

pharmaand GmbH
Taborstrasse 1
1020 Vienna, Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/294/013 (PVC/CTFE/alu blisters)
EU/1/04/294/027 (PVC/PVDC/alu blisters)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Emselex 7.5 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Emselex 7.5 mg prolonged-release tablets
darifenacin

2. NAME OF THE MARKETING AUTHORISATION HOLDER

pharma& *[logo]*

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON OF UNIT PACK

1. NAME OF THE MEDICINAL PRODUCT

Emselex 15 mg prolonged-release tablets
darifenacin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 15 mg darifenacin (as hydrobromide).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

7 tablets
14 tablets
28 tablets
49 tablets
56 tablets
98 tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Keep the blister packs in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

pharmaand GmbH
Taborstrasse 1
1020 Vienna, Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/294/007	7 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/008	14 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/009	28 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/010	49 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/011	56 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/012	98 tablets (PVC/CTFE/alu blisters)
EU/1/04/294/021	7 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/022	14 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/023	28 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/024	49 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/025	56 tablets (PVC/PVDC/alu blisters)
EU/1/04/294/026	98 tablets (PVC/PVDC/alu blisters)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Emselex 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACKS (INCLUDING BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Emselex 15 mg prolonged-release tablets
darifenacin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 15 mg darifenacin (as hydrobromide).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

140 tablets
Multipack comprising 10 packs, each containing 14 tablets.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Keep the blister packs in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

pharmaand GmbH
Taborstrasse 1
1020 Vienna, Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/294/014 (PVC/CTFE/alu blisters)
EU/1/04/294/028 (PVC/PVDC/alu blisters)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Emselex 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON OF MULTIPACKS (WITHOUT BLUE BOX)

1. NAME OF THE MEDICINAL PRODUCT

Emselex 15 mg prolonged-release tablets
darifenacin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each tablet contains 15 mg darifenacin (as hydrobromide).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

14 tablets
Component of a multipack, not to be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Keep the blister packs in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

pharmaand GmbH
Taborstrasse 1
1020 Vienna, Austria

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/04/294/014 (PVC/CTFE/alu blisters)
EU/1/04/294/028 (PVC/PVDC/alu blisters)

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Emselex 15 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

Emselex 15 mg prolonged-release tablets
darifenacin

2. NAME OF THE MARKETING AUTHORISATION HOLDER

pharma& *[logo]*

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Emselex 7.5 mg prolonged-release tablets
Darifenacin

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Emselex is and what it is used for
2. What you need to know before you take Emselex
3. How to take Emselex
4. Possible side effects
5. How to store Emselex
6. Contents of the pack and other information

1. What Emselex is and what it is used for

How Emselex works
Emselex reduces the activity of an overactive bladder. This enables you to wait longer before you go to the toilet and it increases the amount of urine that your bladder can hold.

What Emselex can be used for
Emselex belongs to a class of medicines which relax the muscles of the bladder. It is used in adults for the treatment of the symptoms of overactive bladder conditions - such as a sudden urge to rush to the toilet, needing to go to the toilet frequently and/or not getting to the toilet in time and wetting yourself (urge incontinence).

2. What you need to know before you take Emselex

Do not take Emselex:
- if you are allergic to darifenacin or any of the other ingredients of this medicine (listed in section 6).
- if you suffer from urinary retention (inability to empty your bladder).
- if you have gastric retention (problems emptying the contents of the stomach).
- if you suffer from uncontrolled narrow-angle glaucoma (high pressure in the eyes that is not being adequately treated).
- if you have myasthenia gravis (a disease marked by unusual tiredness and weakness of selected muscles).
- if you have severe ulcerative colitis or toxic megacolon (acute dilation of the colon due to complication of infection or inflammation).
- if you have severe liver problems.
- if you are taking medicines that strongly decrease the activity of some liver enzymes such as ciclosporin (a medicine used in transplantation to prevent organ rejection or for other conditions, e.g. rheumatoid arthritis or atopic dermatitis), verapamil (a medicine used to lower blood pressure, to correct heart rhythm or to treat angina pectoris), antifungal medicines (e.g. ketoconazole and itraconazole) and some antiviral medicines (e.g. ritonavir) see paragraph “Other medicines and Emselex”).

Warnings and precautions
Talk to your doctor before taking Emselex

- if you have autonomic neuropathy (damage to the nerves that communicate between the brain and internal organs, muscles, skin, and blood vessels to regulate vital functions, including the heart rate, blood pressure and bowel function) – your doctor will have told you if you have this.
- if you have a condition where one or more organs in your abdomen has moved up into your chest through a hole in your diaphragm, causing you to get heartburn and belch a lot.
- if you have difficulties in passing urine and a weak stream of urine.
- if you have severe constipation (less than or equal to 2 bowel movements per week).
- if you have a digestive motility disorder.
- if you have an obstructive gastrointestinal disorder (any obstruction of the passage of intestinal or gastric contents, such as narrowing of the pylorus, the lower part of the stomach) – your doctor will have told you if you have this.
- if you are taking medicinal products that can cause or worsen inflammation of the oesophagus such as oral bisphosphonates (a class of medicinal products that prevent the loss of bone mass and are used to treat osteoporosis).
- if you are receiving treatment for narrow-angle glaucoma.
- if you have liver problems.
- if you have urinary tract infection or other kidney problems.
- if you have an overactive muscle that controls the emptying of the bladder which may cause accidental passing of urine (a condition called detrusor hyperreflexia) – your doctor will tell you if you are suffering from this condition.
- if you have heart diseases.

If any of these apply to you, tell your doctor before you take Emselex.

During treatment with Emselex, tell your doctor straight away and stop taking Emselex if you experience swelling of the face, lips, tongue and/or throat (signs of angioedema).

Children and adolescents
Emselex is not recommended for use in children and adolescents (<18 years).

Other medicines and Emselex
Tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This is particularly important if you are taking any of the following as your doctor may need to adjust your dose of Emselex and/or the other medicine:

- certain antibiotics (e.g. erythromycin, clarithromycin, telithromycin and rifampicin),
- antifungal medicines (e.g. ketoconazole and itraconazole - see paragraph “Do not take Emselex”, fluconazole, terbinafine),
- medicines used to reduce the activity of the immune system, for example, after organ transplantation (e.g. ciclosporin - see paragraph “Do not take Emselex”),
- antiviral medicines (e.g. ritonavir - see paragraph “Do not take Emselex”),
- antipsychotic medicines (e.g. thioridazine),
- certain antidepressants (e.g. imipramine and paroxetine),
- certain anticonvulsants (carbamazepine, barbiturates),
- certain medicines used to treat heart problems (e.g. verapamil - see paragraph “Do not take Emselex”, flecainide, digoxin and quinidine),
- certain medicines used for the treatment of stomach problems (e.g. cimetidine),
- other antimuscarinic medicines (e.g. tolterodine, oxybutynin and flavoxate).

Please also inform your doctor if you are taking products containing St John’s wort.

Emselex with food and drink
Eating food has no effect on Emselex. Grapefruit juice may interact with Emselex. Tell your doctor if you are taking grapefruit juice regularly.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.
Emselex is not recommended during pregnancy.
Emselex should be taken with caution while breast-feeding.

Driving and using machines
Emselex may cause effects such as dizziness, blurred vision, trouble sleeping or drowsiness. If you have any of these symptoms whilst taking Emselex, consult your doctor for advice on changing the dose or considering an alternative treatment. You should not drive or use machines if you are affected by these symptoms. For Emselex, these side effects have been reported to be uncommon (see section 4).

3. How to take Emselex

Always take Emselex exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. If you have the impression that the effect of Emselex is too strong or too weak, talk to your doctor or pharmacist.

How much Emselex to take
The recommended starting dose, including for patients aged over 65 years, is 7.5 mg daily. Depending on your response to Emselex, your doctor may increase your dose to 15 mg daily, two weeks after starting therapy.

These doses are suitable for people with mild liver problems or people with kidney problems.

Take Emselex tablets once a day with liquid, at about the same time each day.

The tablet may be taken with or without food. Swallow the tablet whole. Do not chew, split or crush it.

If you take more Emselex than you should
If you have taken more tablets than you have been told to take, or if someone else accidentally takes your tablets, go to your doctor or hospital for advice immediately. When seeking medical advice, make sure that you take this leaflet and your remaining tablets with you to show them to the doctor. People who have taken an overdose may have dry mouth, constipation, headache, indigestion and nasal dryness. Overdose with Emselex may lead to severe symptoms requiring emergency treatment in hospital.

If you forget to take Emselex
If you forget to take Emselex at the usual time, take it as soon as you remember, unless it is the time for your next dose. Do not take a double dose to make up for a forgotten dose.

If you stop taking Emselex
Your doctor will tell you how long your treatment with Emselex will last. Do not stop treatment early because you do not see an immediate effect. Your bladder will need some time to adapt. Finish the course of treatment prescribed by your doctor. If you have not noticed any effect by then, discuss it with your doctor.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The side effects caused by Emselex are usually mild and temporary.

Some side effects could be serious
Not known (frequency cannot be estimated from the available data)
Serious allergic reactions including swelling, mainly of the face and neck (angioedema).

Other side effects
Very common (may affect more than 1 in 10 people)
Dry mouth, constipation.

Common (may affect up to 1 in 10 people)
Headache, abdominal pain, indigestion, feeling sick, dry eyes, nasal dryness.

Uncommon (may affect up to 1 in 100 people)
Fatigue, accidental injury, facial swelling, high blood pressure, diarrhoea, flatulence, ulceration of the mucous membrane of the mouth, increased liver enzymes (this shows abnormal functioning of the liver), swelling including swelling of the hands, ankles or feet, dizziness, sleeplessness, drowsiness, abnormal thinking, runny nose (rhinitis), cough, shortness of breath, dry skin, itching, rash, sweating, visual disturbance including blurred vision, taste disturbance, urinary tract disorder or infection, impotence, discharge and itching in the vagina, bladder pain, inability to empty your bladder.

Not known (frequency cannot be estimated from the available data)
Depressed mood/mood alterations, hallucination.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Emselex

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and blister. The expiry date refers to the last day of that month.
- Keep the blister packs in the outer carton in order to protect from light.
- Do not use if the pack is damaged or shows signs of tampering.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Emselex contains
- The active substance is darifenacin. Each tablet contains 7.5 mg darifenacin (as hydrobromide).
- The other ingredients are calcium hydrogen phosphate (anhydrous), hypromellose, magnesium stearate, polyethylene glycol, titanium dioxide (E171) and talc.

What Emselex looks like and contents of the pack
Emselex 7.5 mg prolonged-release tablets are round, convex white tablets and are debossed with “DF” on one side and “7.5” on the other.

The tablets are available in blister packs containing 7, 14, 28, 49, 56 or 98 tablets or in multipacks containing 140 (10x14) tablets. Not all pack sizes may be available in your country.

Marketing Authorisation Holder
pharmaand GmbH
Taborstrasse 1
1020 Vienna
Austria

Manufacturer
DREHM Pharma GmbH
Grünbergstrasse 15/3/3
1120 Vienna
Austria

This leaflet was last revised in

Other sources of information
Detailed information on this medicine is available on the European Medicines Agency website:
http://www.ema.europa.eu

Package leaflet: information for the user

Emselex 15 mg prolonged-release tablets
Darifenacin

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Talk to your doctor before taking Emselex

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5. How to store Emselex

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- Do not use this medicine after the expiry date which is stated on the carton and blister. The expiry date refers to the last day of that month.
- Keep the blister packs in the outer carton in order to protect from light.
- Do not use if the pack is damaged or shows signs of tampering.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Emselex contains
- The active substance is darifenacin. Each tablet contains 15 mg darifenacin (as hydrobromide).
- The other ingredients are calcium hydrogen phosphate (anhydrous), hypromellose, magnesium stearate, polyethylene glycol, talc, titanium dioxide (E171), red iron oxide (E172) and yellow iron oxide (E172).

What Emselex looks like and contents of the pack
Emselex 15 mg prolonged-release tablets are round, convex light peach tablets and are debossed with "DF" on one side and "15" on the other.

The tablets are available in blister packs containing 7, 14, 28, 49, 56 or 98 tablets or in multipacks containing 140 (10x14) tablets. Not all pack sizes may be available in your country.

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