Beta-blocking agents, for ophthalmic use (alone or in combination with brinzolamide, dorzolamide, brimonidine, travoprost, latanoprost, bimatoprost, pilocarpine) betaxolol - carteolol - levobunolol - metipranolol - timolol and product information on systemic adverse drug reactions after ophthalmic administration.

Final SmPC and PL wording Agreed by the PhVWP in May 2011

Doc.Ref.: CMDh/PhVWP/030/2011
July 2011

Proposed changes in SmPC based on class review of systemic effects of ophthalmic beta-blockers.

Specific text for betaxolol or timolol only is in **bold.**

4.2 POSOLOGY AND METHOD OF ADMINISTRATION		
Carteolol, levobunolol, metipranolol, befunolol	Betaxolol	Timolol
When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.	When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.	When using nasolacrimal occlusion or closing the eyelids for 2 minutes, the systemic absorption is reduced. This may result in a decrease in systemic side effects and an increase in local activity.
4.3 CONTRAINDICATIONS		
Carteolol, levobunolol, metipranolol, befunolol	Betaxolol	Timolol
Hypersensitivity to the active substance (substances), or to any of the excipients.	Hypersensitivity to the active substance (substances), or to any of the excipients.	Hypersensitivity to the active substance (substances), or to any of the excipients.
Reactive airway disease including bronchial asthma or a history of bronchial asthma, severe chronic obstructive pulmonary disease.	**Reactive airway disease including severe bronchial asthma or a history of severe bronchial asthma, severe chronic obstructive pulmonary disease.**	Reactive airway disease including bronchial asthma or a history of bronchial asthma, severe chronic obstructive pulmonary disease.
Sinus bradycardia, sick sinus syndrome, sino-atrial block, second or third degree atrioventricular block not controlled with pace-maker. Overt cardiac failure, cardiogenic shock.	Sinus bradycardia, sick sinus syndrome sino-atrial block, second or third degree atrioventricular block not controlled with pace-maker. Overt cardiac failure, cardiogenic shock.	Sinus bradycardia, sick sinus syndrome sino-atrial block, second or third degree atrioventricular block not controlled with pace-maker. Overt cardiac failure, cardiogenic

		shock.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE		
Carteolol, levobunolol, metipranolol, befunolol	Betaxolol	Timolol
Like other topically applied ophthalmic agents <active substance> is absorbed systemically. Due to beta-adrenergic component, <active substance>, the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic beta-adrenergic blocking agents may occur. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see 4.2.	Like other topically applied ophthalmic agents <active substance> is absorbed systemically. Due to beta-adrenergic component, <active substance>, the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic beta-adrenergic blocking agents may occur. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see 4.2.	Like other topically applied ophthalmic agents <active substance> is absorbed systemically. Due to beta-adrenergic component, <active substance>, the same types of cardiovascular, pulmonary and other adverse reactions seen with systemic beta-adrenergic blocking agents may occur. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. To reduce the systemic absorption, see 4.2.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE		
Cardiac disorders: In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered. Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions. Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block.	*Cardiac disorders:* In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered. Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions. Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block.	*Cardiac disorders:* In patients with cardiovascular diseases (e.g. coronary heart disease, Prinzmetal's angina and cardiac failure) and hypotension therapy with beta-blockers should be critically assessed and the therapy with other active substances should be considered. Patients with cardiovascular diseases should be watched for signs of deterioration of these diseases and of adverse reactions. Due to its negative effect on conduction time, beta-blockers should only be given with caution to patients with first degree heart block.
Vascular disorders Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud's disease or Raynaud's syndrome) should be treated with caution.	*Vascular disorders* Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud's disease or Raynaud's syndrome) should be treated with caution.	*Vascular disorders* Patients with severe peripheral circulatory disturbance/disorders (i.e. severe forms of Raynaud's disease or Raynaud's syndrome) should be treated with caution.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE		
Respiratory disorders: Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some ophthalmic beta-blockers. <*Brand name*> should be used with caution, in patients with mild/moderate chronic obstructive pulmonary disease (COPD) and only if the potential benefit outweighs the potential risk.	*Respiratory disorders:* Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some ophthalmic beta-blockers. **For Betaxolol only:** **Patients with mild/moderate bronchial asthma, a history of mild/moderate bronchial asthma or, mild/moderate chronic obstructive pulmonary disease (COPD) should be treated with caution.**	*Respiratory disorders:* Respiratory reactions, including death due to bronchospasm in patients with asthma have been reported following administration of some ophthalmic beta-blockers. <*Brand name*> should be used with caution, in patients with mild/moderate chronic obstructive pulmonary disease (COPD) and only if the potential benefit outweighs the potential risk.
Hypoglycaemia/diabetes Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as beta-blockers may mask the signs and symptoms of acute hypoglycaemia.	*Hypoglycaemia/diabetes* Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as beta-blockers may mask the signs and symptoms of acute hypoglycaemia.	*Hypoglycaemia/diabetes* Beta-blockers should be administered with caution in patients subject to spontaneous hypoglycaemia or to patients with labile diabetes, as beta-blockers may mask the signs and symptoms of acute hypoglycaemia.
Beta-blockers may also mask the signs of hyperthyroidism.	Beta-blockers may also mask the signs of hyperthyroidism.	Beta-blockers may also mask the signs of hyperthyroidism.
Corneal diseases Ophthalmic β-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.	*Corneal diseases* Ophthalmic β-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.	*Corneal diseases* Ophthalmic β-blockers may induce dryness of eyes. Patients with corneal diseases should be treated with caution.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE		
Other beta-blocking agents The effect on intra-ocular pressure or the known effects of systemic beta-blockade may be potentiated when <active substance> is given to the patients already receiving a systemic beta-blocking agent. The response of these patients should be closely observed. The use of two topical beta-adrenergic blocking agents is not recommended (see section 4.5).	*Other beta-blocking agents* The effect on intra-ocular pressure or the known effects of systemic beta-blockade may be potentiated when <active substance> is given to the patients already receiving a systemic beta-blocking agent. The response of these patients should be closely observed. The use of two topical beta-adrenergic blocking agents is not recommended (see section 4.5).	*Other beta-blocking agents* The effect on intra-ocular pressure or the known effects of systemic beta-blockade may be potentiated when <active substance> is given to the patients already receiving a systemic beta-blocking agent. The response of these patients should be closely observed. The use of two topical beta-adrenergic blocking agents is not recommended (see section 4.5).
Anaphylactic reactions While taking beta-blockers, patients with history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens and unresponsive to the usual dose of adrenaline used to treat anaphylactic reactions.	*Anaphylactic reactions* While taking beta-blockers, patients with history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens and unresponsive to the usual dose of adrenaline used to treat anaphylactic reactions.	*Anaphylactic reactions* While taking beta-blockers, patients with history of atopy or a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge with such allergens and unresponsive to the usual dose of adrenaline used to treat anaphylactic reactions.
Choroidal detachment Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g. timolol, acetazolamide) after filtration procedures.	*Choroidal detachment* Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g. timolol, acetazolamide) after filtration procedures.	*Choroidal detachment* Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g. timolol, acetazolamide) after filtration procedures.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE		
Surgical anaesthesia β-blocking ophthalmological preparations may block systemic β-agonist effects e.g. of adrenaline. The anaesthesiologist should be informed when the patient is receiving <active substance>.	*Surgical anaesthesia* β-blocking ophthalmological preparations may block systemic β-agonist effects e.g. of adrenaline. The anaesthesiologist should be informed when the patient is receiving <active substance>.	*Surgical anaesthesia* β-blocking ophthalmological preparations may block systemic β-agonist effects e.g. of adrenaline. The anaesthesiologist should be informed when the patient is receiving <active substance>.

4.5 INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION		
Carteolol, levobunolol, metipranolol, befunolol	Betaxolol	Timolol
No specific drug interaction studies have been performed with <*active substance*>.	No specific drug interaction studies have been performed with <*active substance*>.	No specific drug interaction studies have been performed with <*active substance*>.
There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blockers solution is administered concomitantly with oral calcium channel blockers, beta-adrenergic blocking agents, antiarrhythmics (including amiodarone), digitalis glycosides, parasympathomimetics, guanethidine.	There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blockers solution is administered concomitantly with oral calcium channel blockers, beta-adrenergic blocking agents, antiarrhythmics (including amiodarone), digitalis glycosides, parasympathomimetics, guanethidine.	There is a potential for additive effects resulting in hypotension and/or marked bradycardia when ophthalmic beta-blockers solution is administered concomitantly with oral calcium channel blockers, beta-adrenergic blocking agents, antiarrhythmics (including amiodarone), digitalis glycosides, parasympathomimetics, guanethidine.
		For timolol only: **Potentiated systemic beta-blockade (e.g., decreased heart rate, myocardial* depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g. quinidine, fluoxetine, paroxetine) and timolol.**
Mydriasis resulting from concomitant use of ophthalmic beta-blockers and adrenaline (epinephrine) has been reported occasionally.	Mydriasis resulting from concomitant use of ophthalmic beta-blockers and adrenaline (epinephrine) has been reported occasionally.	Mydriasis resulting from concomitant use of ophthalmic beta-blockers and adrenaline (epinephrine) has been reported occasionally.

*****_There is the print error in the CMD texts (the word "myocardial" is not included). This error will be corrected._

4.6 FERTILITY, PREGNANCY AND LACTATION		
Carteolol, levobunolol, metipranolol, befunolol	Betaxolol	Timolol
Pregnancy There are no adequate data for the use of <active substance> in pregnant women. <active substance> should not be used during pregnancy unless clearly necessary. To reduce the systemic absorption, see 4.2. Epidemiological studies have not revealed malformative effects but show a risk for intra uterine growth retardation when beta-blockers are administered by the oral route. In addition, signs and symptoms of beta-blockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If <*Brand name*> is administered until delivery, the neonate should be carefully monitored during the first days of life.	*Pregnancy* There are no adequate data for the use of <active substance> in pregnant women. <active substance> should not be used during pregnancy unless clearly necessary. To reduce the systemic absorption, see 4.2. Epidemiological studies have not revealed malformative effects but show a risk for intra uterine growth retardation when beta-blockers are administered by the oral route. In addition, signs and symptoms of beta-blockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If <*Brand name*> is administered until delivery, the neonate should be carefully monitored during the first days of life.	*Pregnancy* There are no adequate data for the use of <active substance> in pregnant women. <active substance> should not be used during pregnancy unless clearly necessary. To reduce the systemic absorption, see 4.2. Epidemiological studies have not revealed malformative effects but show a risk for intra uterine growth retardation when beta-blockers are administered by the oral route. In addition, signs and symptoms of beta-blockade (e.g. bradycardia, hypotension, respiratory distress and hypoglycaemia) have been observed in the neonate when beta-blockers have been administered until delivery. If <*Brand name*> is administered until delivery, the neonate should be carefully monitored during the first days of life.
Lactation Beta-blockers are excreted in breast milk. However, at therapeutic doses of <*active substance*> in eye drops it is not likely that sufficient amounts would be present in breast milk to produce clinical symptoms of beta-blockade in the infant. To reduce the systemic absorption, see 4.2.	*Lactation* Beta-blockers are excreted in breast milk. However, at therapeutic doses of <*active substance*> in eye drops it is not likely that sufficient amounts would be present in breast milk to produce clinical symptoms of beta-blockade in the infant. To reduce the systemic absorption, see 4.2.	*Lactation* Beta-blockers are excreted in breast milk. However, at therapeutic doses of <*active substance*> in eye drops it is not likely that sufficient amounts would be present in breast milk to produce clinical symptoms of beta-blockade in the infant. To reduce the systemic absorption, see 4.2.

4.8 UNDESIRABLE EFFECTS		
Carteolol, levobunolol, metipranolol, befunolol	Betaxolol	Timolol
Like other topically applied ophthalmic drugs, <*active substance*> is absorbed into the systemic circulation. This may cause similar undesirable effects as seen with systemic beta-blocking agents. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers.	Like other topically applied ophthalmic drugs, <*active substance*> is absorbed into the systemic circulation. This may cause similar undesirable effects as seen with systemic beta-blocking agents. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers.	Like other topically applied ophthalmic drugs, <*active substance*> is absorbed into the systemic circulation. This may cause similar undesirable effects as seen with systemic beta-blocking agents. Incidence of systemic ADRs after topical ophthalmic administration is lower than for systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers.
Data from clinical studies including frequencies (if available).		
Additional adverse reactions have been seen with ophthalmic beta-blockers and may potentially occur with <Brand name>:		
Carteolol, levobunolol, metipranolol, befunolol	Betaxolol	Timolol
Immune system disorders: Systemic allergic reactions including angioedema, urticaria, localized and generalized rash, pruritus, anaphylactic reaction.	*Immune system disorders:* Systemic allergic reactions including angioedema, urticaria, localized and generalized rash, pruritus, anaphylactic reaction.	*Immune system disorders:* Systemic allergic reactions including angioedema, urticaria, localized and generalized rash, pruritus,anaphylactic reaction.
Metabolism and nutrition disorders: Hypoglycaemia.	*Metabolism and nutrition disorders:* Hypoglycaemia.	*Metabolism and nutrition disorders:* Hypoglycaemia.
Psychiatric disorders: Insomnia, depression, nightmares, memory loss.	*Psychiatric disorders:* Insomnia, depression, nightmares, memory loss.	*Psychiatric disorders:* Insomnia, depression, nightmares, memory loss.
Nervous system disorders: Syncope, cerebrovascular accident, cerebral ischemia, increases in signs and symptoms of myasthenia gravis, dizziness, paraesthesia, and headache.	*Nervous system disorders:* Syncope, cerebrovascular accident, cerebral ischemia, increases in signs and symptoms of myasthenia gravis, dizziness, paraesthesia, and headache.	*Nervous system disorders:* Syncope, cerebrovascular accident, cerebral ischemia, increases in signs and symptoms of myasthenia gravis, dizziness, paraesthesia, and headache.

Eye disorders: Signs and symptoms of ocular irritation (e.g. burning, stinging, itching, tearing, redness), blepharitis, keratitis, blurred vision and choroidal detachment following filtration surgery (see 4.4 Special warnings and special precautions for use). decreased corneal sensitivity, dry eyes, corneal erosion ptosis, diplopia.	*Eye disorders:* Signs and symptoms of ocular irritation (e.g. burning, stinging, itching, tearing, redness), blepharitis, keratitis, blurred vision and choroidal detachment following filtration surgery (see 4.4 Special warnings and special precautions for use). decreased corneal sensitivity, dry eyes, corneal erosion ptosis, diplopia.	*Eye disorders:* Signs and symptoms of ocular irritation (e.g. burning, stinging, itching, tearing, redness), blepharitis, keratitis, blurred vision and choroidal detachment following filtration surgery (see 4.4 Special warnings and special precautions for use). decreased corneal sensitivity, dry eyes, corneal erosion ptosis, diplopia.
Cardiac disorders: Bradycardia, chest pain, palpitations, oedema, arrhythmia, congestive heart failure, atrioventricular block, cardiac arrest, cardiac failure.	*Cardiac disorders:* Bradycardia, chest pain, palpitations, oedema, arrhythmia, congestive heart failure, atrioventricular block, cardiac arrest, cardiac failure.	*Cardiac disorders:* Bradycardia, chest pain, palpitations, oedema, arrhythmia, congestive heart failure, atrioventricular block, cardiac arrest, cardiac failure.
Vascular disorders: Hypotension, Raynaud's phenomenon, cold hands and feet.	*Vascular disorders:* Hypotension, Raynaud's phenomenon, cold hands and feet.	*Vascular disorders:* Hypotension, Raynaud's phenomenon, cold hands and feet.
Respiratory, thoracic, and mediastinal disorders: Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), dyspnoea, cough.	*Respiratory, thoracic, and mediastinal disorders:* Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), dyspnoea, cough.	*Respiratory, thoracic, and mediastinal disorders:* Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), dyspnoea, cough.
Gastrointestinal disorders: Dysgeusia, nausea, dyspepsia, diarrhoea, dry mouth, abdominal pain, vomiting.	*Gastrointestinal disorders:* Dysgeusia, nausea, dyspepsia, diarrhoea, dry mouth, abdominal pain, vomiting.	*Gastrointestinal disorders:* Dysgeusia, nausea, dyspepsia, diarrhoea, dry mouth, abdominal pain, vomiting.
Skin and subcutaneous tissue disorders: Alopecia, psoriasiform rash or exacerbation of psoriasis, skin rash.	*Skin and subcutaneous tissue disorders:* Alopecia, psoriasiform rash or exacerbation of psoriasis, skin rash.	*Skin and subcutaneous tissue disorders:* Alopecia, psoriasiform rash or exacerbation of psoriasis, skin rash.

Musculoskeletal and connective tissue disorders: Myalgia.	*Musculoskeletal and connective tissue disorders:* Myalgia.	*Musculoskeletal and connective tissue disorders:* Myalgia.
Reproductive system and breast disorders: Sexual dysfunction, decreased libido.	*Reproductive system and breast disorders:* Sexual dysfunction, decreased libido.	*Reproductive system and breast disorders:* Sexual dysfunction, decreased libido.
General disorders and administration site conditions: Asthenia/fatigue.	*General disorders and administration site conditions:* Asthenia/fatigue.	*General disorders and administration site conditions:* Asthenia/fatigue.

PACKAGE LEAFLET
Version 1, 10.6.2011
2. BEFORE YOU USE <Brand name>
Do not use <Brand name, pharmaceutical form > eye drops solution
- if you are allergic to <active substance>, beta-blockers or any of the other ingredients.
- if you have now or have had in past respiratory problems such as asthma, severe chronic obstructive bronchitis.

For Betaxolol only
- if you have now or have had in past respiratory problems such as severe asthma, severe chronic obstructive bronchitis
- if you have a slow heart beat, heart failure or disorders of heart rhythm.

Take special care with <Brand name>.
Before you use this medicine, tell your doctor if you have now or have had in the past
- coronary heart disease, heart failure, hypotension,
- disturbances of heart rate as bradycardia
- breathing problems, asthma or chronic obstructive pulmonary disease
- peripheral arterial disease as Raynaud's disease or Raynaud's syndrome)
- diabetes as <active substance> may mask signs and symptoms of low blood sugar
- overactivity of the thyroid gland as <active substance> may mask signs and symptoms

Tell your doctor before surgical anaesthesia that you are using **<Brand name>** as <active substance> may change effects of some medicines used during anaesthesia.
Using other medicines
<Brand name> can affect or be affected by other medicines you are using, including other eye drops for the treatment of glaucoma. Tell your doctor if you are using or intend to use medicines to lower blood pressure, heart medicine or medicines to treat diabetes. Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.
Pregnancy and breast-feeding
Do not use <Brand name> if you are pregnant unless your doctor considers it necessary.
Do not use <Brand name> if you are breast-feeding. <Active substance> may get into your milk**.**
Ask your doctor for advice before taking any medicine during breast-feeding.
3. HOW TO USE <Brand name>.
Always use <Brand name> eye drops solution exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.
After using <Brand name>, press a finger into the corner of your eye, by the nose (picture X) by 2 minutes. This helps to stop <active substance> getting into the rest of the body.
4. POSSIBLE SIDE EFFECTS
Like all medicines <Brand name, pharmaceutical form> can cause side effects although not everybody gets them.
You can usually carry on taking the drops, unless the effects are serious. If you're worried, talk to a

doctor or pharmacist. Do not stop using <Brand name> without speaking to your doctor.
The frequency of possible side effects listed below is defined using the following convention
Very common (affects more than 1 user in 10)
Common (affects 1 to 10 users in 100)
Uncommon (affects 1 to 10 users in 1,000)
Rare (affects 1 to 10 users in 10,000)
Not known (frequency cannot be estimated from the available data)

#Product specific side effect should be placed here# #

Like other topically applied ophthalmic drugs, *<active substance>* is absorbed into the blood. This may cause similar side effects as seen with systemic beta-blocking agents. Incidence of side effects after topical ophthalmic administration is lower than for systemic administration. Listed adverse reactions include reactions seen within the class of ophthalmic beta-blockers:
Systemic allergic reactions including angioedema, urticaria, localized and generalized rash, pruritus, anaphylactic reaction.
Hypoglycaemia.
Insomnia, depression, nightmares, memory loss.
Syncope, cerebrovascular accident, cerebral ischemia, increases in signs and symptoms of myasthenia gravis, dizziness, paraesthesia, and headache.
Signs and symptoms of ocular irritation (e.g. burning, stinging, itching, tearing, redness), blepharitis, keratitis, blurred vision and choroidal detachment following filtration surgery, decreased corneal sensitivity, dry eyes, corneal erosion, ptosis, diplopia.
Bradycardia, chest pain, palpitations, oedema, arrhythmia, congestive heart failure, atrioventricular block, cardiac arrest, cardiac failure.
Hypotension, Raynaud's phenomenon, cold hands and feet.
Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), dyspnoea, cough.
Dysgeusia, nausea, dyspepsia, diarrhoea, dry mouth, abdominal pain, vomiting.
Alopecia, psoriasiform rash or exacerbation of psoriasis, skin rash.
Myalgia.
Sexual dysfunction, decreased libido.
Asthenia/fatigue.
If any of the side effects get serious, or if you notice any side effects not mentioned in this leaflet, please, tell your doctor or pharmacist.