RISK MANAGEMENT PLAN

Active substance(s) (INN or common name):	Fexofenadine hydrochloride
Pharmaco-therapeutic group (ATC Code):	Antihistamines for systemic use (R06AX26)
Name of Marketing Authorisation Holder or Applicant:	Cipla Europe NV
Number of medicinal products to which this RMP refers:	02
Product(s) concerned (brand name(s)):	1. Fexofenadine Cipla 120 mg film-coated tablet 2. Fexofenadine Cipla 180 mg film-coated tablet

Data lock point for this RMP: 15October 2013

Version no: 01

Date of final sign off: 02 February 2018

PART I: PRODUCT(S) OVERVIEW

Part	**Module/annex**	**Date last updated for submission (sign off date)**	***Version number of RMP when last submitted/ or Not Applicable**
Part II Safety Specification	SV Post authorisation experience Only required for updates to the RMP		Not Applicable
	SVIII Summary of the safety concerns		Not Applicable
Part III Pharmacovigilance Plan	Only needed if reference product has additional PhV activities		Not Applicable
Part IV Plan for post-authorisation efficacy studies	Only needed if reference product has imposed post-authorisation efficacy studies		Not Applicable
Part V Risk Minimisation Measures		12-Aug-2014	01
Part VI Summary of RMP		12-Aug-2014	01
Part VII Annexes	ANNEX 2 Current or proposed SmPC/PIL	12-Aug-2014	01
	ANNEX 3 Worldwide marketing status by country		Not Applicable
	ANNEX 5		Not

Part	**Module/annex**	**Date last updated for submission (sign off date)**	***Version number of RMP when last submitted/ or Not Applicable**
	Synopsis of pharmacoepidemiological study programme		Applicable
	ANNEX 6 Protocols for proposed and on-going studies in Part III		Not Applicable
	ANNEX 7 Specific adverse event follow-up forms		Not Applicable
	ANNEX 8 Protocols for studies in Part IV		Not Applicable
	ANNEX 9 Synopsis of newly available study reports in Parts III-IV		Not Applicable
	ANNEX 10 Details of proposed additional risk minimisation activities		Not Applicable
	ANNEX 11 Mock up examples		Not Applicable
	ANNEX 12 Other supporting data		Not Applicable

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Overview of versions:

Version number of last agreed RMP: Not applicable

Version number: 02

Agreed within: Decentralised procedure

Current RMP versions under evaluation:

RMP Version number	**Submitted on**	**Submitted within**
Not applicable	Not applicable	Not applicable

Invented name(s) in the European Economic Area (EEA)	1. Fexofenadine Cipla 120 mg film-coated tablet 2. Fexofenadine Cipla 180 mg film-coated tablet
Authorisation procedure	Decentralised procedure
Brief description of the product:	Fexofenadine hydrochloride belongs to the class of antihistamines for systemic use. Fexofenadine hydrochloride is a non-sedating H1 antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.
Indication(s) in the EEA	**Current**: Fexofenadine Cipla120 mg is indicated in adults and adolescents 12 years and older for the relief of symptoms associated with seasonal allergic rhinitis. Fexofenadine cipla 180 mg is indicated in adults and adolescents 12 years and older for the relief of symptoms associated with chronic idiopathic urticaria.
	Proposed: Not applicable
Posology and route of administration in the EEA	**Proposed**: <u>Fexofenadine 120 mg</u>: ***Adults*** The recommended dose of fexofenadine hydrochloride for adults is 120 mg once daily taken before a meal. Fexofenadine is a pharmacologically active metabolite of terfenadine. ***Paediatric population*** • Adolescents aged 12 years and over The recommended dose of fexofenadine hydrochloride for adolescentsaged 12 years and over is 120 mg one daily taken before a meal.

	• Children under 12 years of age The efficacy and safety of fexofenadine hydrochloride 120 mg in children under 12 has not been studied. ***Special populations*** Studies in special risk groups (older people, renally or hepatically impaired patients) indicate that it is not necessary to adjust the dose of fexofenadine hydrochloride in these patients. <u>Fexofenadine 180 mg</u>: ***Adults*** The recommended dose of fexofenadine hydrochloride for adults is 180 mg once daily taken before a meal. Fexofenadine is a pharmacologically active metabolite of terfenadine. ***Paediatric population*** • Adolescents aged 12 years and over The recommended dose of fexofenadine hydrochloride for adolescents aged 12 years and over is 180 mg one daily taken before a meal. • Children under 12 years of age The efficacy and safety of fexofenadine hydrochloride 180 mg in children under 12 has not been studied. ***Special populations*** Studies in special risk groups (older people, renally or hepatically impaired patients) indicate that it is not necessary to adjust the dose of fexofenadine hydrochloride in these patients.

	Proposed: Not applicable
Pharmaceutical form(s) and strengths	**Current**: <u>Fexofenadine 120 mg</u>: Film-coated tablet Peach coloured, oblong, biconvex, in dimension, film coated tablet plain on both sides. Dimension: 15.00 mm x 6.5 mm <u>Fexofenadine 180 mg</u> Film-coated tablet Yellow coloured, oblong, biconvex, film coated tablet plain on one side with a central score line on the other side. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses. Dimension: 17.00 x 8.00 mm
	Proposed: Not applicable

Country and date of first authorisation worldwide: Unknown, 11-Mar-1996

Country and date of first launch worldwide:

Country and date of first authorisation in the EEA: Unknown, 11-Mar-1996

Is the product subject to additional monitoring in the EU? Yes ☐ No ☑

PART II: MODULE SV– POST-AUTHORISATION EXPERIENCE

SV.1 Action taken by regulatory authorities and/or marketing authorisation holders for safety reasons

No actions have been taken by regulatory authorities and/or marketing authorisation holders for safety concerns.

SV.2 Non-study post-authorisation exposure

There is no non-study post-authorisation exposure, since the product is not yet marketed.

SV.3 Post-authorisation use in special populations

There is no post-authorisation use in special population, since the product is not yet marketed

SV.4 Post-authorisation off-label use

There is no post-authorisation off-label use, since the product is not yet marketed

SV.5 Epidemiological study exposure (if applicable)

Cipla Europe NV has not conducted any epidemiological study, hence there is no epidemiological study exposure.

PART II: MODULE SVIII - SUMMARY OF THE SAFETY CONCERNS

Table 3: Summary of safety concerns

Summary of safety concerns	
Important identified risks	• Cardiovascular events(tachycardia, palpitations) • Hypersensitivityincluding anaphylactic reactions • Co-administration with erythromycin or ketoconazole
Important potential risks	• None
Missing information	• Use in elderly and patients with impaired renal or hepatic function • Use in pregnantor breast feeding women

PART III: PHARMACOVIGILANCE PLAN

Not applicable.

PART IV: PLANS FOR POST-AUTHORISATION EFFICACY STUDIES

Cipla Europe NV does not have plans for post authorisation efficacy studies.

PART V: RISK MINIMISATION MEASURES

V.1 Risk minimisation measures by safety concern

Safety concern	**Cardiovascular events**
Objective(s) of the risk minimisation measures	To minimise the occurrence of cardiovascular events(tachycardia, palpitations)
Routine risk minimisation measures	Cardiac disorder such as tachycardia and palpitations have been reported in clinical trials. Risk of cardiovascular events has been mentioned in section 4.4 (special warnings and precautions) and section 4.8 (Undesirable effects) of SPC as well as in Section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) and section 4 (Possible side effects) of PIL. As per section 4.4 (special warnings and precautions) of SPC, patients with history of cardiovascular disorders should be warned for possibility of palpitations and tachycardia. As per Section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) of PIL, the patients should inform their physicians if they have history of cardiovascular disorders.
Additional risk minimisation measure(s) (repeat as necessary)	None.

Safety concern	**Hypersensitivityincluding anaphylactic reactions**
Objective(s) of the risk minimisation measures	To minimise the occurrence of hypersensitivity

Safety concern	**Hypersensitivityincluding anaphylactic reactions**
Routine risk minimisation measures	Hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis have been reported in clinical trials. Risk of hypersensitivity reactions has been mentioned in section 4.3 (contraindications) and 4.8 (Undesirable effects) of SPC as well as in Section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) and section 4 (Possible side effects) of PIL. As per section 4.3 (Contraindications) of SPC and section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) of PIL, fexofenadine is contraindicated in patients with known hypersensitivity to fexofenadine.
Additional risk minimisation measure(s) (repeat as necessary)	None.

Safety concern	**Co-administration with erythromycin or ketoconazole**
Objective(s) of the risk minimisation measures	To minimise the co-administration with erythromycin or ketoconzole

Safety concern	**Co-administration with erythromycin or ketoconazole**
Routine risk minimisation measures	Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole has been found to result in a 2-3 times increase in the level of fexofenadine in plasma. The changes were not accompanied by any effects on the QT interval and were not associated with any increase in adverse reactions compared to the medicinal products given singly. The risk of interaction due to Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole has been mentioned in section 4.5 (Interaction with other medicinal products and other forms of interaction) of SPC. Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole should be avoided.
Additional risk minimisation measure(s) (repeat as necessary)	None.

Important potential risk : None

Missing information:

Safety concern	Use in elderly and patients with impaired renal or hepatic function
Objective(s) of the risk minimisation measures	To minimise the use of fexofenadine in elderly and patients with impaired renal or hepatic function

Safety concern	Use in elderly and patients with impaired renal or hepatic function
Routine risk minimisation measures	This risk has been mentioned in the section 4.4 (special warnings and precautions for use). As with most new medicinal products, there is only limited data in the older people and renally or hepatically impaired patients. Fexofenadine hydrochloride should be administered with care in these special groups.
Additional risk minimisation measure(s) (repeat as necessary)	None.

Safety concern	Use in pregnantor breast feeding women
Objective(s) of the risk minimisation measures	To minimise the use of fexofenadine in pregnantor breast feeding women
Routine risk minimisation measures	This risk has been mentioned in the section 4.6 (Fertility, pregnancy and lactation). There are no adequate data from the use of fexofenadine hydrochloride in pregnant women. Limited animal studies do not indicate direct or indirect harmful effects with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development. Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary. There are no data on the content of human milk after administering fexofenadine hydrochloride. However, when terfenadine was administered to nursing mothers fexofenadine was found to cross into human

Safety concern	Use in pregnantor breast feeding women
	breast milk. Therefore fexofenadine hydrochloride is not recommended for mothers breast-feeding their babies.
Additional risk minimisation measure(s) (repeat as necessary)	None.

Effectiveness of risk minimisation measures	
How effectiveness of risk minimisation measures for the safety concern will be measured	Not applicable
Criteria for judging the success of the proposed risk minimisation measures	Not applicable
Planned dates for assessment	Not applicable
Results of effectiveness measurement	Not applicable
Impact of risk minimisation	Not applicable
Comment	Not applicable

V.2 Risk minimisation measure failure (if applicable)

Not applicable

V.3 Summary table of risk minimisation measures

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
Cardiovascular events(tachycardia, palpitations)	Cardiac disorder such as tachycardia and palpitations have been reported in clinical trials. Risk of cardiovascular	None.

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
	events has been mentioned in section 4.4 (special warnings and precautions) and section 4.8 (Undesirable effects) of SPC as well as in Section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) and section 4 (Possible side effects) of the PIL. As per section 4.4 (special warnings and precautions) of SPC, patients with history of cardiovascular disorders should be warned for possibility of palpitations and tachycardia. As per Section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) of PIL, the patients should inform their physicians if they have history of cardiovascular disorders.	
Hypersensitivityincluding anaphylactic reactions	Hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis have been reported in clinical trials. Risk of	None.

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	hypersensitivity reactions has been mentioned in section 4.3 (contraindications) and 4.8 (Undesirable effects) of SPC as well as in Section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) and section 4 (Possible side effects) of the PIL. As per section 4.3 (Contraindications) of SPC and section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) of the PIL, fexofenadine is contraindicated in patients with known hypersensitivity to fexofenadine.	
Co-administration with erythromycin or ketoconazole	Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole has been found to result in a 2-3 times increase in the level of fexofenadine in plasma. The changes were not accompanied by any effects on the QT interval and were not associated with any	None

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
	increase in adverse reactions compared to the medicinal products given singly. The risk of interaction due to Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole has been mentioned in section 4.5 (Interaction with other medicinal products and other forms of interaction) of SPC. Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole should be avoided.	
Use in elderly and patients with impaired renal or hepatic function	This risk has been mentioned in the section 4.4 (special warnings and precautions for use). As with most new medicinal products, there is only limited data in the older people and renally or hepatically impaired patients. Fexofenadine hydrochloride should be administered with care in these special groups.	None
Use in pregnantor breast feeding women	This risk has been mentioned in the section 4.6 (Fertility, pregnancy and lactation).	None

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	There are no adequate data from the use of fexofenadine hydrochloride in pregnant women. Limited animal studies do not indicate direct or indirect harmful effects with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development. Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary. There are no data on the content of human milk after administering fexofenadine hydrochloride. However, when terfenadine was administered to nursing mothers fexofenadine was found to cross into human breast milk. Therefore fexofenadine hydrochloride is not recommended for mothers breast-feeding their babies.	

PART VI: SUMMARY OF THE RISK MANAGEMENT PLAN BY PRODUCT

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Summary of safety concerns	
Important identified risks	• Cardiovascular events(tachycardia, palpitations) • Hypersensitivityincluding anaphylactic reactions • Co-administration with erythromycin or ketoconazole
Important potential risks	• None
Missing information	• Use in elderly and patients with impaired renal or hepatic function • Use in pregnantor breast feeding women

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Study/activity Type, title and category (1-3)	**Objectives**	**Safety concerns addressed**	**Status (planned, started)**	**Date for submission of interim or final reports (planned or actual)**
Not applicable	Not applicable	Not applicable	Not applicable	Not applicable

VI.1.3 Summary of Post authorisation efficacy development plan

Not applicable.

VI.1.4 Summary table of Risk Minimisation Measures

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
Cardiovascular events(tachycardia, palpitations),	Cardiac disorder such as tachycardia and palpitations have been reported in clinical trials. Risk of cardiovascular events has been mentioned in section 4.4 (special warnings and precautions) and section 4.8 (Undesirable effects) of SPC as well as in Section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) and section 4 (Possible side effects) of the PIL. As per section 4.4 (special warnings and precautions) of SPC, patients with history of cardiovascular disorders should be warned for possibility of palpitations and tachycardia. As per Section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) of PIL, the patients should inform their physicians if they have history of cardiovascular disorders.	None.
Hypersensitivityincluding anaphylactic reactions	Hypersensitivity reactions with manifestations such as angioedema, chest tightness,	None.

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	dyspnoea, flushing and systemic anaphylaxis have been reported in clinical trials. Risk of hypersensitivity reactions has been mentioned in section 4.3 (contraindications) and 4.8 (Undesirable effects) of SPC as well as in Section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) and section 4 (Possible side effects) of the PIL. As per section 4.3 (Contraindications) of SPC and section 2 (What you need to know before you take Fexofenadine hydrochloride tablets) of the PIL, fexofenadine is contraindicated in patients with known hypersensitivity to fexofenadine.	
Co-administration with erythromycin or ketoconazole	Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole has been found to result in a 2-3 times increase in the level of fexofenadine in plasma. The	None

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	changes were not accompanied by any effects on the QT interval and were not associated with any increase in adverse reactions compared to the medicinal products given singly. The risk of interaction due to Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole has been mentioned in section 4.5 (Interaction with other medicinal products and other forms of interaction) of SPC. Co-administration of fexofenadine hydrochloride with erythromycin or ketoconazole should be avoided.	
Use in elderly and patients with impaired renal or hepatic function	This risk has been mentioned in the section 4.4 (special warnings and precautions for use). As with most new medicinal products, there is only limited data in the older people and renally or hepatically impaired patients. Fexofenadine hydrochloride should be administered with	None

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	care in these special groups.	
Use in pregnantor breast feeding women	This risk has been mentioned in the section 4.6 (Fertility, pregnancy and lactation). There are no adequate data from the use of fexofenadine hydrochloride in pregnant women. Limited animal studies do not indicate direct or indirect harmful effects with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development. Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary. There are no data on the content of human milk after administering fexofenadine hydrochloride. However, when terfenadine was administered to nursing mothers fexofenadine was found to cross into human breast milk. Therefore fexofenadine hydrochloride is not recommended for mothers breast-feeding their	None

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures
	babies.	

VI.2 Podsumowanie planu zarządzania ryzykiem dla produktu leczniczego Fexofenadine hydrochloride Cipla przeznaczone do publicznej wiadomości

VI.2.1 Omówienie rozpowszechnienia choroby

Sezonowe alergiczne zapalenie błony śluzowej nosa (katar sienny):

Sezonowe alergiczne zapalenie błony śluzowej nosa (katar sienny) to stan zapalny górnych dróg oddechowych występujący w odpowiedzi na ekspozycję na czynniki wywołujące reakcję alergiczną (alergeny), takie jak drzewa, trawy i pyłki chwastów. Sezonowe alergiczne zapalenie błony śluzowej nosa jest najczęściej wywoływane przez pyłki unoszące się w powietrzu w różnych porach roku w różnych częściach kraju. Do objawów sezonowego alergicznego zapalenia błony śluzowej nosa należy wyciek z nosa, świąd nosa, kichanie i/lub niedrożność nosa.

Sezonowe alergiczne zapalenie błony śluzowej nosa dotyka jedną na sześć osób[1]. Największą chorobowość na sezonowe alergiczne zapalenie błony śluzowej nosa odnotowuje się w wieku młodzieńczym i wczesnej dorosłości i nie ma różnicy w częstości występowania tego schorzenia między płciami[2].

Przewlekła pokrzywka idiopatyczna:

Pokrzywka to rodzaj wysypki skórnej charakteryzującej się bladoczerwonymi, wypukłymi, swędzącymi guzkami. Pokrzywka może również powodować uczucie pieczenia lub kłucia. Jeśli pokrzywka utrzymuje się dłużej niż sześć tygodni i jej przyczyna jest nieznana, określa się ją mianem przewlekłej pokrzywki idiopatycznej. Może być bolesna i powodować powstawanie bąbli. Przewlekła pokrzywka idiopatyczna może być również wynikiem nieprawidłowej odpowiedzi organizmu na substancje i tkanki, które naturalnie występują w organizmie (reakcja autoimmunologiczna).

Przewlekła pokrzywka idiopatyczna jest częstym schorzeniem skóry, które dotyka 0,1-3% osób w USA i Europie i stanowi prawie 75% wszystkich przypadków przewlekłej pokrzywki[3].

VI.2.2 Podsumowanie korzyści wynikających z leczenia

Nie dotyczy.

VI.2.3 Niewiadome związane z korzyściami z leczenia

- Nie ma odpowiednich danych dotyczących stosowania feksofenadyny chlorowodorku u kobiet w ciąży. Nie ma danych na temat zawartości feksofenadyny chlorowodorku w mleku kobiecym po podaniu leku.
- Nie ma odpowiednich danych dotyczących stosowania feksofenadyny u osób w podeszłym wieku i pacjentów z upośledzoną czynnością nerek lub wątroby.

VI.2.4 Podsumowanie niepokojących kwestii dotyczących bezpieczeństwa

Istotne zidentyfikowane zagrożenia

Zagrożenie	**Co już wiadomo**	**Możliwość zapobiegania**
Zaburzenia serca (zdarzenia sercowo-naczyniowe, takie jak przyspieszone bicie serca (tachykardia) i palpitacje serca)	W badaniach klinicznych obserwowano zaburzenia serca, takie jak nieprawidłowe, szybkie bicie serca (tachykardia) i uczucie kołatania serca (palpitacje).	Tak. Zagrożenia związane z zaburzeniami serca zostały wymienione w punkcie 2 (Informacje ważne przed zastosowaniem feksofenadyny chlorowodorku w postaci tabletek) i punkcie 4 (Możliwe działania niepożądane) ulotki dołączonej do opakowania. Zgodnie z punktem 2 (Informacje ważne przed zastosowaniem feksofenadyny chlorowodorku w postaci tabletek) ulotki dołączonej do opakowania pacjent powinien poinformować lekarza, jeżeli występowały u

Zagrożenie	Co już wiadomo	Możliwość zapobiegania
		niego schorzenia serca w przeszłości.
Reakcje alergiczne (reakcje nadwrażliwości) łącznie z reakcjami anafilaktycznymi	W badaniach klinicznych obserwowano reakcje alergiczne (reakcje nadwrażliwości) objawiające się m.in. ciężką pokrzywką(obrzęk naczynioruchowy), uczuciem ściskania w klatce piersiowej, trudnościami z oddychaniem (duszność), zaczerwienieniem twarzy i reakcją alergiczną całego organizmu (anafilaksja układowa).	Tak. Zagrożenia związane z reakcjami alergicznymi zostały wymienione w punkcie 2 (Informacje ważne przed zastosowaniem feksofenadyny chlorowodorku w postaci tabletek) i punkcie 4 (Możliwe działania niepożądane) ulotki dołączonej do opakowania. Zgodnie z punktem 2 (Informacje ważne przed zastosowaniem feksofenadyny chlorowodorku w postaci tabletek) ulotki dołączonej do opakowania stosowanie feksofenadyny jest przeciwwskazane u pacjentów ze stwierdzonym uczuleniem na feksofenadynę.
Jednoczesne stosowanie z erytromycyną lub ketokonazolem	Wykazano, że jednoczesne stosowanie feksofenadyny chlorowodorku z erytromycyną lub ketokonazolem powoduje 2–3-krotne zwiększenie stężenia feksofenadyny we	Tak. Należy poinformować pacjentów i lekarzy, aby unikać jednoczesnego stosowania feksofenadyny chlorowodorku z erytromycyną lub ketokonazolem.

Zagrożenie	Co już wiadomo	Możliwość zapobiegania
	krwi (osoczu). Zmiany te nie miaływpływu na odstęp QT w badaniu elektrokardiograficznym i nie wiązały się ze zwiększeniem częstości występowania działań niepożądanych w porównaniu z sytuacją, gdy każdy z tych produktów leczniczych podawany był oddzielnie.	

<u>Istotne potencjalne zagrożenia</u>:

Zagrożenie	Co już wiadomo (w tym powód, dla którego dane zagrożenie uznano za potencjalne zagrożenie)
Brak	

<u>Brakujące informacje</u>:

Zagrożenie	Co już wiadomo
Stosowanie u osób w podeszłym wieku i pacjentów mających problemy z nerkami lub wątrobą (pacjenci z upośledzoną czynnością nerek lub wątroby)	Tak jak w przypadku większości nowych produktów leczniczych, dane dotyczące stosowania feksofenadyny u pacjentów w podeszłym wieku oraz u pacjentów mających problemy z nerkami lub wątrobą (pacjenci z upośledzoną czynnością nerek lub wątroby) są ograniczone. Należy zachować ostrożność stosując feksofenadyny chlorowodorek w tych szczególnych grupach pacjentów. Badania z udziałem pacjentów należących do szczególnych grup ryzyka (osoby w podeszłym wieku, pacjenci z upośledzoną czynnością nerek lub wątroby) wykazują, że nie ma konieczności dostosowywania dawki feksofenadyny chlorowodorku w tych grupach pacjentów.
Kobiety w ciąży i karmiące	Nie ma odpowiednich danych dotyczących stosowania

Zagrożenie	**Co już wiadomo**
piersią	feksofenadyny chlorowodorku u kobiet w ciąży. Ograniczone badania na zwierzętach nie wykazują bezpośredniego lub pośredniego szkodliwego wpływu na przebieg ciąży, rozwój zarodka/płodu, przebieg porodu lub rozwój pourodzeniowy. Nie należy stosować feksofenadyny chlorowodorku w okresie ciąży, jeśli nie jest to bezwzględnie konieczne. Nie ma danych na temat zawartości feksofenadyny chlorowodorku w mleku kobiecym po podaniu leku. Jednak kiedy podawano terfenadynę matkom karmiącym piersią, stwierdzano przenikanie feksofenadyny do mleka matki. W związku z tym nie zaleca się stosowania feksofenadyny chlorowodorku u kobiet karmiących piersią.

VI.2.5 Podsumowanie środków minimalizujących ryzyko w odniesieniu do określonych zagrożeń

Nie dotyczy.

VI.2.6 Przewidywany plan rozwoju po wydaniu pozwolenia

Nie dotyczy.

PART VII: ANNEXES

Table of contents

Annex 1 – EudraVigilance Interface

Not applicable.

Annex 2 - SmPC& Package Leaflet

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fexofenadine Cipla 120 mg film-coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 120 mg fexofenadine hydrochloride
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

Peach coloured, oblong, biconvex, in dimension, film coated tablet plain on both sides.
Dimension: 15.00 mm x 6.5 mm

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Fexofenadine Cipla120 mg is indicated in adults and adolescents 12 years and older for the relief of symptoms associated with seasonal allergic rhinitis.

4.2. Posology and method of administration

Posology

Adults
The recommended dose of fexofenadine hydrochloride for adults is 120 mg once daily taken before a meal.

Fexofenadine is a pharmacologically active metabolite of terfenadine.

Paediatric population

- Adolescents aged 12 years and over
  The recommended dose of fexofenadine hydrochloride for adolescentsaged 12 years and over is 120 mg one daily taken before a meal.

- Children under 12 years of age
  The efficacy and safety of fexofenadine hydrochloride 120 mg in children under 12 has not been studied.

Special populations

Studies in special risk groups (older people, renally or hepatically impaired patients) indicate that it is not necessary to adjust the dose of fexofenadine hydrochloride in these patients.

4.3. Contraindications

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

4.4. Special warning and precautions for use

As with most new medicinal products, there is only limited data in the older people and renally or hepatically impaired patients. Fexofenadine hydrochloride should be administered with care in these special groups.

Patients with a history of or ongoing cardiovascular disease should be warned that, antihistamines as a medicine class, have been associated with the adverse reactions, tachycardia and palpitations (see section 4.8).

4.5. Interactions with other medicinal products and other forms of Interaction

Fexofenadine does not undergo hepatic biotransformation and therefore will not interact with other medicinal products through hepatic mechanisms. Coadministration of fexofenadine hydrochloride with erythromycin or ketoconazole has been found to result in a 2-3 times increase in the level of fexofenadine in plasma. The changes were not accompanied by any effects on the QT interval and were not associated with any increase in adverse reactions compared to the medicinal products given singly.

Animal studies have shown that the increase in plasma levels of fexofenadine observed after coadministration of erythromycin or ketoconazole, appears to be due to an increase in gastrointestinal absorption and either a decrease in biliary excretion or gastrointestinal secretion, respectively.

No interaction between fexofenadine and omeprazole was observed. However, the administration of an antacid containing aluminium and magnesium hydroxide gels 15 minutes prior to fexofenadine hydrochloride caused a reduction in bioavailability, most likely due to binding in the gastrointestinal tract. It is advisable to leave 2 hours between administration of fexofenadine hydrochloride and aluminium and magnesium hydroxide containing antacids.

4.6. Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of fexofenadine hydrochloride in pregnant women. Limited animal studies do not indicate direct or indirect harmful effects with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3). Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary.

Breast-feeding
There are no data on the content of human milk after administering fexofenadine hydrochloride. However, when terfenadine was administered to nursing mothers fexofenadine was found to cross into human breast milk. Therefore fexofenadine hydrochloride is not recommended for mothers breast-feeding their babies.

4.7. Effects on ability to drive and use machines

On the basis of the pharmacodynamic profile and reported adverse reactions it is unlikely that fexofenadine hydrochloride tablets will produce an effect on the ability to drive or use machines. In objective tests, fexofenadine hydrochloride has been shown to have no significant effects on central nervous system function. This means that patients may drive or perform tasks that require concentration. However, in order to identify sensitive people who have an unusual reaction to medicinal products, it is advisable to check the individual response before driving or performing complicated tasks.

4.8. Undesirable effects

The following frequency rating has been used, when applicable:
Very common ≥1/10; Common ≥1/100 and <1/10; Uncommon ≥1/1,000 and <1/100; Rare ≥1/10,000 and <1/1,000; Very rare <1/10,000 and not known (frequency cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

In adults, the following undesirable effects have been reported in clinical trials, with an incidence similar to that observed with placebo:

Nervous system disorders
Common: headache, drowsiness, dizziness

Gastrointestinal disorders
Common: nausea

General disorders and administration site conditions
Uncommon: fatigue

In adults, the following undesirable effects have been reported in post-marketing surveillance. The frequency with which they occur is not known (cannot be estimated from available data):

Immune system disorders
Hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis

Psychiatric disorders
Insomnia, nervousness, sleep disorders or nightmares/excessive dreaming (paroniria)

Cardiac disorders
Tachycardia, palpitations

Gastrointestinal disorders
Diarrhoea

Skin and subcutaneous tissue disorders
Rash, urticaria, pruritus

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.

[To be completed nationally]

4.9. Overdose

Dizziness, drowsiness, fatigue and dry mouth have been reported with overdose of fexofenadine hydrochloride. Single doses up to 800 mg and doses up to 690 mg twice daily for 1 month or 240 mg once daily for 1 year have been administered to healthy subjects without the development of clinically significant adverse reactions as compared with placebo. The maximum tolerated dose of fexofenadine hydrochloride has not been established.

Standard measures should be considered to remove any unabsorbed medicinal product. Symptomatic and supportive treatment is recommended. Haemodialysis does not effectively remove fexofenadine hydrochloride from blood.

No specific antidote is known.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

*Pharmacotherapeuticgroup:*Antihistamines for systemic use. *ATC code:*R06A X26.

Mechanism of action
Fexofenadine hydrochloride is a non-sedating H_1antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.

Clinical efficacy and safety
Human histamine wheal and flare studies following single and twice daily doses of fexofenadine hydrochloride demonstrate that the medicinal product exhibits an antihistaminic effect beginning within one hour, achieving maximum at 6 hours and lasting 24 hours. There was no evidence of tolerance to these effects after 28 days of dosing. A positive dose-response relationship between doses of 10 mg to 130 mg taken orally was found to exist. In this model of antihistaminic activity, it was found that doses of at least 130 mg were required to achieve a consistent effect that was maintained over a 24 hour period. Maximum inhibition in skin wheal and flare areas were greater than 80%.

No significant differences in QT_c intervals were observed in seasonal allergic rhinitis patients given fexofenadine hydrochloride up to 240 mg twice daily for 2 weeks when compared to placebo. Also, no significant change in QT_c intervals was observed in healthy subjects given fexofenadine hydrochloride up to 60 mg twice daily for 6 months, 400 mg twice daily for 6.5 days and 240 mg once daily for 1 year, when compared to placebo. Fexofenadine at concentrations 32 times greater than the therapeutic concentration in man had no effect on the delayed rectifier K+ channel cloned from human heart.

Fexofenadine hydrochloride (5-10 mg/kg po) inhibited antigen induced bronchospasm in sensitised guinea pigs and inhibited histamine release at supratherapeutic concentrations (10-100 μM) from peritoneal mast cells.

5.2. Pharmacokinetic Properties

*Absorption:*Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with T_{max} occurring at approximately 1-3 hours post dose. The mean C_{max} value was approximately 427 ng/ml following the administration of a 120 mg dose once daily.

*Distribution:*Fexofenadine is 60-70% plasma protein bound.

*Biotrasformation and elimination:*Fexofenadine undergoes negligible metabolism (hepatic or non-hepatic), as it was the only major compound identified in urine and faeces of animals and man. The plasma concentration profiles of fexofenadine follow a bi-exponential decline with a terminal elimination half-life ranging from 11 to 15 hours after multiple dosing. The single and multiple dose pharmacokinetics of fexofenadine are linear for oral doses up to 120 mg BID. A dose of 240 mg BID produced slightly greater than proportional increase (8.8%) in steady state area under the curve, indicating that fexofenadine pharmacokinetics are practically linear at these doses between 40 mg and 240 mg taken daily. The major route of elimination is believed to be via biliary excretion while up to 10% of ingested dose is excreted unchanged through the urine.

5.3. Preclinical Safety Data

Dogs tolerated 450 mg/kg administered twice daily for 6 months and showed no toxicity other than occasional emesis. Also, in single dose dog and rodent studies, no treatment-related gross findings were observed following necropsy.

Radiolabelled fexofenadine hydrochloride in tissue distribution studies of the rat indicated that fexofenadine did not cross the blood brain barrier.

Fexofenadine hydrochloride was found to be non-mutagenic in various *in vitro* and *in vivo* mutagenicity tests.

The carcinogenic potential of fexofenadine hydrochloride was assessed using terfenadine studies with supporting pharmacokinetic studies showing fexofenadine hydrochloride exposure (via plasma AUC values). No evidence of carcinogenicity was observed in rats and mice given terfenadine (up to 150 mg/kg/day).

In a reproductive toxicity study in mice, fexofenadine hydrochloride did not impair fertility, was not teratogenic and did not impair pre- or postnatal development.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Tablet core
Microcrystalline Cellulose
Maize Starch
CroscarmelloseSodium
Povidone
Magnesium Stearate

Film coating
Hypromellose
Titanium Dioxide (E171)
Macrogol
Iron oxide yellow (E172)
Iron OxideRed (E172)

6.2. Incompatibilities

Not applicable

6.3. Shelf life

2 years

6.4. Special precautions for storage

This medicinal product does not require any special storage conditions

6.5. Nature and contents of container

PVC/PVDC/Al blisters, packaged into cardboard boxes. 7, 10, 15, 20, 30, 50, 100 and 200 (as 10x20) tablets per package.

Not all packs sizes may be marketed

6.6. Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

For – SE, DE, ES, PT, IT, FR, DK, PL, NO, HU, SI, HR
Cipla Europe NV
Uitbreidingstraat 80, 2600 Antwerp
Belgium

For - FI
Orion Corporation,
Orionintie 1, FI-02200, Espoo
Finland

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF THE FIRST AUTHORISATION /RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Fexofenadine Cipla 180 mg film-coated tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film coated tablet contains 180 mg fexofenadine hydrochloride
For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet

Yellow coloured, oblong, biconvex, film coated tablet plain on one side with a central score line on the other side. The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses. Dimension: 17.00 x 8.00 mm

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Fexofenadine cipla 180 mg is indicated in adults and adolescents 12 years and older for the relief of symptoms associated with chronic idiopathic urticaria.

4.2. Posology and method of administration

Posology

Adults
The recommended dose of fexofenadine hydrochloride for adults is 180 mg once daily taken before a meal.

Fexofenadine is a pharmacologically active metabolite of terfenadine.

Paediatric population
- Adolescents aged 12 years and over

The recommended dose of fexofenadine hydrochloride for adolescents aged 12 years and over is 180 mg one daily taken before a meal.

- Children under 12 years of age

The efficacy and safety of fexofenadine hydrochloride 180 mg in children under 12 has not been studied.

Special populations
Studies in special risk groups (older people, renally or hepatically impaired patients) indicate that it is not necessary to adjust the dose of fexofenadine hydrochloride in these patients.

4.3. Contraindications

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

4.4. Special warning and precautions for use

As with most new medicinal products, there is only limited data in the older people and renally or hepatically impaired patients. Fexofenadine hydrochloride should be administered with care in these special groups.

Patients with a history of or ongoing cardiovascular disease should be warned that, antihistamines as a medicine class, have been associated with the adverse reactions, tachycardia and palpitations (see section 4.8).

4.5. Interactions with other medicinal products and other forms of Interaction

Fexofenadine does not undergo hepatic biotransformation and therefore will not interact with other medicinal products through hepatic mechanisms. Coadministration of fexofenadine hydrochloride with erythromycin or ketoconazole has been found to result in a 2-3 times increase in the level of fexofenadine in plasma. The changes were not accompanied by any effects on the QT interval and were not associated with any increase in adverse reactions compared to the medicinal products given singly.

Animal studies have shown that the increase in plasma levels of fexofenadine observed after co administration of erythromycin or ketoconazole, appears to be due to an increase in gastrointestinal absorption and either a decrease in biliary excretion or gastrointestinal secretion, respectively.

No interaction between fexofenadine and omeprazole was observed. However, the administration of an antacid containing aluminium and magnesium hydroxide gels 15 minutes prior to fexofenadine hydrochloride caused a reduction in bioavailability, most likely due to binding in the gastrointestinal tract. It is advisable to leave 2 hours between administration of fexofenadine hydrochloride and aluminium and magnesium hydroxide containing antacids.

4.6. Fertility, pregnancy and lactation

Pregnancy
There are no adequate data from the use of fexofenadine hydrochloride in pregnant women. Limited animal studies do not indicate direct or indirect harmful effects with respect to effects on pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3). Fexofenadine hydrochloride should not be used during pregnancy unless clearly necessary.

Breast-feeding
There are no data on the content of human milk after administering fexofenadine hydrochloride. However, when terfenadine was administered to nursing mothers fexofenadine was found to cross into human breast milk. Therefore fexofenadine hydrochloride is not recommended for mothers breast-feeding their babies.

4.7. Effects on ability to drive and use machines

On the basis of the pharmacodynamic profile and reported adverse reactions it is unlikely that fexofenadine hydrochloride tablets will produce an effect on the ability to drive or use machines. In objective tests, fexofenadine hydrochloride has been shown to have no

significant effects on central nervous system function. This means that patients may drive or perform tasks that require concentration. However, in order to identify sensitive people who have an unusual reaction to medicinal products, it is advisable to check the individual response before driving or performing complicated tasks.

4.8. Undesirable effects

The following frequency rating has been used, when applicable:
Very common ≥1/10; Common ≥1/100 and <1/10; Uncommon ≥1/1,000 and <1/100; Rare ≥1/10,000 and <1/1,000; Very rare <1/10,000 and not known (frequency cannot be estimated from the available data).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

In adults, the following undesirable effects have been reported in clinical trials, with an incidence similar to that observed with placebo:

Nervous system disorders
Common: headache, drowsiness, dizziness

Gastrointestinal disorders
Common: nausea

General disorders and administration site conditions
Uncommon: fatigue

In adults, the following undesirable effects have been reported in post-marketing surveillance. The frequency with which they occur is not known (can not be estimated from available data):

Immune system disorders
Hypersensitivity reactions with manifestations such as angioedema, chest tightness, dyspnoea, flushing and systemic anaphylaxis

Psychiatric disorders
Insomnia, nervousness, sleep disorders or nightmares/excessive dreaming (paroniria)

Cardiac disorders
Tachycardia, palpitations

Gastrointestinal disorders
Diarrhoea

Skin and subcutaneous tissue disorders
Rash, urticaria, pruritus

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.

[To be completed nationally]

4.9. Overdose

Dizziness, drowsiness, fatigue and dry mouth have been reported with overdose of fexofenadine hydrochloride. Single doses up to 800 mg and doses up to 690 mg twice daily for 1 month or 240 mg once daily for 1 year have been administered to healthy subjects without the development of clinically significant adverse reactions as compared with placebo. The maximum tolerated dose of fexofenadine hydrochloride has not been established.

Standard measures should be considered to remove any unabsorbed medicinal product. Symptomatic and supportive treatment is recommended. Haemodialysis does not effectively remove fexofenadine hydrochloride from blood.

No specific antidote is known.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

*Pharmacotherapeuticgroup:*Antihistamines for systemic use. *ATC code:*R06A X26.

Mechanism of action
Fexofenadine hydrochloride is a non-sedating H_1antihistamine. Fexofenadine is a pharmacologically active metabolite of terfenadine.

Clinical efficacy and safety
Human histamine wheal and flare studies following single and twice daily doses of fexofenadine hydrochloride demonstrate that the medicinal product exhibits an antihistaminic effect beginning within one hour, achieving maximum at 6 hours and lasting 24 hours. There was no evidence of tolerance to these effects after 28 days of dosing. A positive dose-response relationship between doses of 10 mg to 130 mg taken orally was found to exist. In this model of antihistaminic activity, it was found that doses of at least 130 mg were required to achieve a consistent effect that was maintained over a 24 hour period. Maximum inhibition in skin wheal and flare areas were greater than 80%.

No significant differences in QT_c intervals were observed in seasonal allergic rhinitis patients given fexofenadine hydrochloride up to 240 mg twice daily for 2 weeks when compared to placebo. Also, no significant change in QT_c intervals was observed in healthy subjects given fexofenadine hydrochloride up to 60 mg twice daily for 6 months, 400 mg twice daily for 6.5 days and 240 mg once daily for 1 year, when compared to placebo. Fexofenadine at concentrations 32 times greater than the therapeutic concentration in man had no effect on the delayed rectifier K+ channel cloned from human heart.

Fexofenadine hydrochloride (5-10 mg/kg po) inhibited antigen induced bronchospasm in sensitised guinea pigs and inhibited histamine release at supratherapeutic concentrations (10-100 μM) from peritoneal mast cells.

5.2. Pharmacokinetic Properties

*Absorption:*Fexofenadine hydrochloride is rapidly absorbed into the body following oral administration, with T_{max} occurring at approximately 1-3 hours post dose. The mean C_{max} value was approximately 494 ng/ml following the administration of a 180 mg dose once daily.

*Distribution:*Fexofenadine is 60-70% plasma protein bound.

*Biotransformation and elimination:*Fexofenadine undergoes negligible metabolism (hepatic or non-hepatic), as it was the only major compound identified in urine and faeces of animals and man. The plasma concentration profiles of fexofenadine follow a bi-exponential decline with a terminal elimination half-life ranging from 11 to 15 hours after multiple dosing. The single and multiple dose pharmacokinetics of fexofenadine are linear for oral doses up to 120 mg BID. A dose of 240 mg BID produced slightly greater than proportional increase (8.8%) in steady state area under the curve, indicating that fexofenadine pharmacokinetics are practically linear at these doses between 40 mg and 240 mg taken daily. The major route of elimination is believed to be via biliary excretion while up to 10% of ingested dose is excreted unchanged through the urine.

5.3. Preclinical Safety Data

Dogs tolerated 450 mg/kg administered twice daily for 6 months and showed no toxicity other than occasional emesis. Also, in single dose dog and rodent studies, no treatment-related gross findings were observed following necropsy.

Radiolabelled fexofenadine hydrochloride in tissue distribution studies of the rat indicated that fexofenadine did not cross the blood brain barrier.

Fexofenadine hydrochloride was found to be non-mutagenic in various *in vitro* and *in vivo* mutagenicity tests.

The carcinogenic potential of fexofenadine hydrochloride was assessed using terfenadine studies with supporting pharmacokinetic studies showing fexofenadine hydrochloride exposure (via plasma AUC values). No evidence of carcinogenicity was observed in rats and mice given terfenadine (up to 150 mg/kg/day).

In a reproductive toxicity study in mice, fexofenadine hydrochloride did not impair fertility, was not teratogenic and did not impair pre- or postnatal development.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Tablet core
Microcrystalline Cellulose
Maize Starch
CroscarmelloseSodium
Povidone
Magnesium Stearate

Film coating
Hypromellose
Titanium Dioxide (E171)
Macrogol
Iron oxide yellow (E172)

6.2. Incompatibilities

Not applicable

6.3. Shelf life

2 years

6.4. Special precautions for storage

This medicinal product does not require any special storage conditions

6.5. Nature and contents of container

PVC/PVDC/Al blisters, packaged into cardboard boxes. 10, 15, 20, 30, 50, 100 and 200 (as 10x20) tablets per package.

Not all packs sizes may be marketed

6.6. Special precautions for disposal

No special requirements

7. MARKETING AUTHORISATION HOLDER

Cipla Europe NV
Uitbreidingstraat 80, 2600 Antwerp,
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF THE FIRST AUTHORISATION /RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

Package leaflet: Information for the patient
Fexofenadine Cipla 120 mg film-coated tablet
Fexofenadine Hydrochloride

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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to 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 Fexofenadine Cipla is and what it isused for

Fexofenadine Cipla contain fexofenadine hydrochloride, which is anantihistamine.

Fexofenadine Cipla 120 mg is used in adults and adolescents of 12 yearsand older to relieve the symptoms that occur with hay fever(seasonal allergic rhinitis) such as sneezing, itchy, runny orblocked nose and itchy, red and watery eyes.

2. What you need to know before you take Fexofenadine Cipla

Do not take Fexofenadine Cipla
- if you are allergic to fexofenadine or any of the otheringredients of this medicine (listed in section 6)

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking Fexofenadine Cipla

Tell your doctor, pharmacist or nurse especially if:
- you have problems with the way your liver or kidneys work;
- you have or ever had heart disease, since this kind ofmedicine may lead to a fast or irregular heart beat;
- you are elderly

Children

Fexofenadine Cipla is not recommended in children below 12 years of age.

Other medicines and Fexofenadine Cipla
Tell your doctor or pharmacist if you are taking, haverecently taken or might take any other medicines.
Indigestion remedies containing aluminium and magnesium, which may affect the action of Fexofenadine Cipla, by lowering the amount ofmedicinal product absorbed.

It is recommended that you leave about 2 hours between thetime that you take Fexofenadine Ciplaand your indigestion remedy.

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 or pharmacist for advice before taking this medicine.
Do not take Fexofenadine Ciplaif you are pregnant, unless necessary.
Fexofenadine Ciplaare not recommended during breast-feeding.

Driving and using machines
Fexofenadine Cipla is unlikely to affect your ability to drive or operatemachinery. However, you should check that these tablets donot make you feel sleepy or dizzy before driving or operatingmachinery.

3. How to take Fexofenadine Cipla

Always take this medicine exactly as your doctor has told you.Check with your doctor or pharmacist if you are not sure.

For adults and adolescents aged 12 years and over
The recommended dose is one tablet (120 mg) daily.
Take your tablet with water before a meal.

Fexofenadine Cipla is not recommended in children below 12 years of age.

If you take more Fexofenadine Ciplathan you should
If you take too many tablets, contact your doctor or thenearest hospital emergency department immediately.

Symptoms of an overdose in adults are dizziness, drowsiness,fatigue and dry mouth.

If you forget to take Fexofenadine Cipla
Do not take a double dose to make up for a forgotten tablet.
Take the next dose at the usual time as prescribed by your doctor.

If you stop taking Fexofenadine Cipla
Tell your doctor if you want to stop taking Fexofenadine Cipla before youhave finished your course of treatment.
If you stop taking Fexofenadine Cipla earlier than planned, yoursymptoms may return.
If you have any further questions on the use of thismedicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects,although not everybody gets them.

Tell your doctor immediately and stop taking Fexofenadine Ciplaifyou experience:

- Swelling of the face, lips, tongue or throat and difficultybreathing, as these may be signs of a serious allergicreaction.

Common side effects (may affect up to 1 in 10 people):
- Headache
- Drowsiness
- Feeling sick (nausea)
- Dizziness.

Uncommon side effects (may affect up to 1 in 100 people):
- Tiredness
- Sleepiness

Additional side effects which may occur are:
- Difficulty sleeping (insomnia)
- Sleeping disorders
- Bad dreams
- Nervousness
- Fast or irregular heart beat
- Diarrhoea
- Skin rash and itching
- Hives
- Serious allergic reactions which can cause swelling of theface, lips, tongue or throat, flushing, chest tightness, anddifficulty breathing.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist ornurse. This includes any possible side effects not listed in thisleaflet.You can also report side effects directly(see details below)**.**By reporting side effects you can help provide moreinformation on the safety of this medicine.

[To be completed nationally]

5. How to store Fexofenadine Cipla

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/label/ blister after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage condition.

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 Fexofenadine Ciplacontains:
- The active substance(s) is(are) fexofenadine hydrochloride. Each film coated tablet contains 120 mg of fexofenadine hydrochloride
- The other ingredients(s)is(are):
  -Tablet core:
  microcrystallinecellulose , maize starch, croscarmellose sodium, povidone, magnesium stearate

-Film coating:
hypromellose, titanium dioxide (E171), macrogol, iron oxide yellow (E172), iron oxide red (E172)

What Fexofenadine Ciplalooks like and contents of the pack

Fexofenadine Cipla 20 mg are peach coloured, oblong, biconvex, film coated tablets plain on both sides. Dimension:15.00 mm x 6.5 mm

PVC/PVDC/Al blisters, packaged into cardboard boxes. 7, 10, 15, 20, 30, 50, 100 and 200 (as 10x20) tablets per package.

Not all packs sizes may be marketed

This medicinal product is authorised in the Member States of the EEA under the following names

Marketing Authorisation Holder and Manufacturer:

Marketing Authorisation Holder

For – SE,DE, ES, PT, IT, FR, DK, PL, NO, HU, SI, HR
Cipla Europe NV
Uitbreidingstraat 80, 2600 Antwerp, Belgium

For - FI
Orion Corporation, Orionintie 1, FI-02200, Espoo Finland

Manufacturer

For – SE, DE, ES, PT, IT, FR, DK, PL, NO, HU, SI, HR

S&D Pharma CZ,
spol. s r.o, Theodor 28, Pchery (Pharmosa.s. facility), 27308, CeskáRepublika

Cipla (EU) Limited
4th Floor, 1 Kingdom Street, London, W26BY, United Kingdom

For - FI
Orion Corporation, Orion Pharma, Orionintie 1, FI-02200, Espoo ,Finland

This leaflet was last revised in MM/YYYY

Package leaflet: Information for the patient
Fexofenadine Cipla 180 mg film-coated tablet
Fexofenadine Hydrochloride

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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

7. What Fexofenadine Cipla is and what it is used for

Fexofenadine Ciplacontain fexofenadine hydrochloride, which is anantihistamine.

Fexofenadine Cipla 180 mg is used in adults and adolescents of 12 yearsand older to relieve the symptoms that occurwith long termallergic skin reactions (chronic idiopathic urticaria) such asitching, swelling and rashes.

8. What you need to know before you take Fexofenadine Cipla

Do not take Fexofenadine Cipla:

- if you are allergic to fexofenadine or any of the otheringredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking Fexofenadine Cipla.

Tell your doctor, pharmacist or nurse especially if:

- you have problems with the way your liver or kidneys work;
- you have or ever had heart disease, since this kind ofmedicine may lead to a fast or irregular heart beat;
- you are elderly.

Children
Fexofenadine Cipla is not recommended in children below 12 years of age.

Other medicines and Fexofenadine Cipla
Tell your doctor or pharmacist if you are taking, haverecently taken or might take any other medicines.

Indigestion remedies containing aluminium and magnesiummay affect the action of Fexofenadine Cipla, by lowering the amount ofmedicinal product absorbed.

It is recommended that you leave about 2 hours between thetime that you take Fexofenadine Cipla and your indigestion remedy.

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 or pharmacist for advice before taking this medicine.

Do not take Fexofenadine Cipla if you are pregnant, unless necessary.
Fexofenadine Cipla is not recommended during breast-feeding.

Driving and using machines
Fexofenadine Cipla is unlikely to affect your ability to drive or operatemachinery. However, you should check that these tablets donot make you feel sleepy or dizzy before driving or operatingmachinery.

9. How to take Fexofenadine Cipla

Always take this medicine exactly as your doctor has told you.Check with your doctor or pharmacist if you are not sure.

For adults and adolescents aged 12 years and over
The recommended dose is one tablet (180 mg) daily.

Take your tablet with water before a meal.

Fexofenadine Cipla is not recommended in children below 12 years of age.

If you take more Fexofenadine Cipla than you should
If you take too many tablets, contact your doctor or thenearest hospital emergency department immediately.

Symptoms of an overdose in adults are dizziness, drowsiness,fatigue and dry mouth.

If you forget to take Fexofenadine Cipla
Do not take a double dose to make up for a forgotten tablet.
Take the next dose at the usual time as prescribed by your doctor.

If you stop taking Fexofenadine Cipla
Tell your doctor if you want to stop taking Fexofenadine Cipla before youhave finished your course of treatment.

If you stop taking Fexofenadine Cipla earlier than planned, yoursymptoms may return.

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

10. Possible side effects

Like all medicines, this medicine can cause side effects,although not everybody gets them.

Tell your doctor immediately and stop taking Fexofenadine Cipla if you experience:
- Swelling of the face, lips, tongue or throat and difficultybreathing, as these may be signs of a serious allergicreaction.

Common side effects (may affect up to 1 in 10 people):
- Headache
- Drowsiness
- Feeling sick (nausea)
- Dizziness

Uncommon side effects (may affect up to 1 in 100 people):
- Tiredness
- Sleepiness.

Additional side effects (frequency not known: cannot beestimated from the available data) which may occur are:
- Difficulty sleeping (insomnia)
- Sleeping disorders
- Bad dreams
- Nervousness
- Fast or irregular heart beat
- Diarrhoea
- Skin rash and itching
- Hives
- Serious allergic reactions which can cause swelling of theface, lips, tongue or throat, flushing, chest tightness, anddifficulty breathing.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist ornurse. This includes any possible side effects not listed in thisleaflet.You can also report side effects directly(see details below).By reporting side effects you can help provide moreinformation on the safety of this medicine.

[To be completed nationally]

11. How to store Fexofenadine Cipla

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is statedon the carton/label/blister after EXP. The expiry date refers to the last dayof that month.

This medicine does not require any special storage condition.

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 helpprotect the environment.

12. Contents of the pack and other information

What Fexofenadine Cipla contains:
- The active substance(s) is (are) fexofenadine hydrochloride. Each tablet contains 180 mg of fexofenadine hydrochloride.

- The other ingredient(s)is (are):
  -Tablet core:
  microcrystalline cellulose, maize starch, croscarmellose sodium, povidone, magnesium stearate

  -Film coating:
  hypromellose, titanium dioxide (E171), macrogol, iron oxide yellow (E172)

What Fexofenadine Cipla looks like and contents of the pack

Fexofenadine Cipla 180 mg areyellow coloured, oblong, film coated tablets plain on one side with a central score line on the other side. Dimension :17.00 x 8.00 mm

PVC/PVDC/Al blisters, packaged into cardboard boxes. 10, 15, 20, 30, 50, 100 and 200 (as 10x20) tablets per package.

Not all packs sizes may be marketed

This medicinal product is authorised in the Member States of the EEA under the following names

Marketing Authorisation Holder
Cipla Europe NV
Uitbreidingstraat 80, 2600 Antwerp, Belgium

Manufacturer
S&D Pharma CZ,
spol. sr.o, Theodor 28, Pchery (Pharmosa.s. facility), 27308, CeskáRepublika

Cipla (EU) Limited
4th Floor, 1 Kingdom Street, London, W26BY, United Kingdom

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Annex 3 - Worldwide marketing authorisation by country (including EEA)

A3.1 Licensing status in the EEA: Cipla Europe NV does not have authorisation of fexofenadine in EEA

Country	**Current licence status**	**Date of licence action**	**Date first marketed in country**	**Brand name(s)**	**Comments**
Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable

A3.2 Licensing status in the rest of the world: Cipla Europe NV does not have authorisation of fexofenadine in rest of the world.

Country	**Current licence status**	**Date of licence action**	**Date first marketed in country**	**Brand name(s)**	**Comments**
Not applicable	Not applicable	Not applicable	Not applicable	Not applicable	Not applicable

Annex 4 - Synopsis of on-going and completed clinical trial programme

Not applicable

Annex 5 - Synopsis of on-going and completed pharmacoepidemiological study programme

Not applicable

Annex 6 - Protocols for proposed and on-going studies in categories 1-3 of the section "Summary table of additional pharmacovigilance activities" in RMP part III

Not applicable

Annex 7 - Specific adverse event follow-up forms

Not applicable

Annex 8 - Protocols for proposed and on-going studies in RMP part IV

Not applicable

Annex 9 - Newly available study reports for RMP parts III & IV

Not applicable

Annex 10 - Details of proposed additional risk minimisation measures (if applicable)

Not applicable

Annex 11 - Mock-up of proposed additional risk minimisation measures (if applicable)

Not applicable

Annex 12 - Other supporting data (including referenced material)

1. Emanuel M. Hay fever, a post industrial revolution epidemic: a history of its growth during the 19th century. Clin Allergy 1988;18:295-304.
2. Parikh A, Scadding G. Seasonal allergic rhinitis. BMJ 1997; 314: 1392- 1395.
3. Negro-Alvarez JM, Miralles-López JC. Chronic idiopathic urticaria treatment. AllergolImmunopathol (Madr). 2001 Jul-Aug;29(4):129-32.