

**ANNEX I**

**SUMMARY OF PRODUCT CHARACTERISTICS**

## **1. NAME OF THE MEDICINAL PRODUCT**

ACOMPLIA 20 mg film-coated tablets

## **2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each tablet contains 20 mg rimonabant.

Excipients:

The tablets contain approx. 115 mg lactose.

For a full list of excipients, see section 6.1.

## **3. PHARMACEUTICAL FORM**

Film-coated tablet

Biconvex, teardrop-shaped, white tablets debossed with “20” on one side.

## **4. CLINICAL PARTICULARS**

### **4.1 Therapeutic indications**

As an adjunct to diet and exercise for the treatment of obese patients ( $\text{BMI} \geq 30 \text{ kg/m}^2$ ), or overweight patients ( $\text{BMI} > 27 \text{ kg/m}^2$ ) with associated risk factor(s), such as type 2 diabetes or dyslipidaemia (see section 5.1).

### **4.2 Posology and method of administration**

In adults, the recommended dosage is one 20 mg tablet daily to be taken in the morning before breakfast.

The treatment should be introduced with a mildly reduced calorie diet.

The safety and efficacy of rimonabant have not been evaluated beyond 2 years.

- **Special Populations**

*Elderly:*

No dosage adjustment is required in elderly (see section 5.2). ACOMPLIA should be used with caution in patients over 75 years of age (see section 4.4).

*Patients with hepatic insufficiency:*

No dosage adjustment is required for patients with mild or moderate hepatic impairment. ACOMPLIA should be used with caution in patients with moderate hepatic impairment. ACOMPLIA should not be used in patients with severe hepatic impairment (see section 4.4 and 5.2).

*Patients with renal impairment:*

No dosage adjustment is required for patients with mild and moderate renal impairment (see section 5.2). ACOMPLIA should not be used in patients with severe renal impairment (see section 4.4 and 5.2).

#### *Paediatrics:*

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

### **4.3 Contraindications**

Hypersensitivity to the active substance or to any of the excipients  
Lactation.

### **4.4 Special warnings and precautions for use**

Rimonabant is metabolised by the liver, thus caution is advised in patients with moderate hepatic impairment. The pharmacokinetics and safety of rimonabant have not been studied in patients with severe hepatic impairment; its use in these patients is not recommended.

There are limited data in patients with moderate renal impairment and no data in patients with severe renal impairment. Rimonabant should not be used in patients with severe renal impairment (see section 4.2 and 5.2).

The efficacy and safety of rimonabant treatment in patients over 75 years of age has not sufficiently been established. Rimonabant should be used with caution in this population (see section 5.2).

Rimonabant has not been studied in patients being treated for epilepsy. In clinical trials no difference in the incidence of seizures was seen in patients receiving rimonabant or placebo. Rimonabant, however, should be used with caution in these patients, see also section 5.3.

The clinical effect (weight loss) of rimonabant in Black patients was lower than in Caucasians. This could be caused by a higher rimonabant clearance than in Caucasians resulting in a lower exposure (see section 5.2).

Rimonabant should be used with caution in combination with potent CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, ritonavir, telithromycin, clarithromycin, nefazodone)(see section 4.5).

Since ACOMPLIA tablets contain lactose, patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption, should not take this medicine.

Patients should be instructed not to increase their dose of ACOMPLIA.

Obesity is a condition that can be associated with depression or other psychiatric conditions. Depressive disorders have been reported in patients receiving rimonabant 20 mg (see section 4.8). Therapy with rimonabant should not be initiated in patients with uncontrolled serious psychiatric illness such as a major depression. Appropriate treatment of this condition should be initiated first and therapy with rimonabant considered once this psychiatric condition is controlled. As there is limited data in patients with antidepressant medication in combination with rimonabant, use of rimonabant is not recommended in these patients.

Patients who had a cardiovascular event (myocardial infarction, stroke, etc.) less than 6 months ago were excluded in the studies for rimonabant.

### **4.5 Interaction with other medicinal products and other forms of interaction**

Rimonabant is metabolized by both CYP3A and amidohydrolase (predominantly hepatic) pathways *in vitro*. Co-administration of CYP3A4 inhibitors will lead to increased exposure of rimonabant. Co-administration of CYP3A4 inducers is expected to reduce the exposure of rimonabant.

**Potential for other medicinal products to affect rimonabant:**

Concomitant administration of ketoconazole (a potent CYP3A4 inhibitor) increased rimonabant AUC by 104% (95% prediction interval: 40% - 197%). A similar increase in exposure is expected with other potent CYP3A4 inhibitors. Caution is advised during concomitant use of ACOMPLIA and potent CYP3A4 inhibitors (e.g. ketoconazole, itraconazole, ritonavir, telithromycin, clarithromycin, nefazodone).

Although concomitant administration of CYP3A4 inducers (e.g. rifampicin, phenytoin, phenobarbital, carbamazepine, St John's wort) has not been studied, it is expected that concomitant administration of potent CYP3A4 inducers may reduce the plasma concentration of rimonabant and may result in loss of efficacy.

Co-administration of orlistat, ethanol or lorazepam had no significant effect on the plasma levels of rimonabant.

**Potential for rimonabant to affect other medicinal products:**

The *in vivo* inhibitory effect on CYP2C8 has not been studied. However, *in vitro*, rimonabant had a mild inhibitory effect on CYP2C8. The potential for inhibition of CYP2C8 *in vivo* appears to be low. Rimonabant does not inhibit or induce other CYP enzymes or P-glycoprotein (P-gp) *in vitro*. This was confirmed clinically with specific probe studies using midazolam (CYP 3A4 substrate) and warfarin (CYP 2C9 substrate) and digoxin (a P-gp substrate).

The steady-state pharmacokinetics of an ethinyl estradiol/levonorgestrel combination oral contraceptive were not significantly altered by concomitant administration of rimonabant.

**4.6 Pregnancy and lactation**

There are no adequate or well-controlled studies in pregnant women. Animal data are inconclusive but suggest possible deleterious effects on embryonal/foetal development (see section 5.3). The potential risk for humans is unknown. Use in pregnancy is, therefore, not recommended. Patients should notify their physician if they become pregnant during treatment with ACOMPLIA.

Rimonabant has been detected in the milk of lactating rats and rimonabant may inhibit the suckling reflex. It is not known if rimonabant is excreted in human milk. ACOMPLIA is contraindicated during breast-feeding (see section 4.3).

**4.7 Effects on ability to drive and use machines**

No studies on the effects on the ability to drive and use machines have been performed. Cognitive investigations in clinical pharmacology studies demonstrated that rimonabant is devoid of any significant cognitive or sedative effect.

**4.8 Undesirable effects**

ACOMPLIA 20 mg has been evaluated for safety in approximately 2500 patients enrolled in studies that examined the metabolic and weight loss effects in overweight and obese patients and in approximately 3800 patients in other indications. In placebo-controlled studies, the discontinuation rate due to adverse reactions was 15.7 % for patients receiving rimonabant. The most common adverse reactions resulting in discontinuation were: nausea, mood alteration with depressive symptoms, depressive disorders, anxiety and dizziness.

Depressive disorders were reported in 3.2% of obese patients, or overweight patients with associated risk factor(s) treated with rimonabant 20 mg. These were usually mild or moderate in severity and resulted in recovery in all cases either after corrective treatment or discontinuation of rimonabant and did not exhibit any differentiating characteristics compared to cases reported in the control groups.

The following table shows all treatment-emergent adverse reactions from four placebo-controlled studies in patients treated for weight loss and related metabolic disorders when these incidences were

statistically significantly greater than the corresponding placebo rate (for events  $\geq 1\%$ ) or considered clinically relevant (for events  $< 1\%$ ).

Classification of expected frequencies of undesirable effects:

Very common ( $\geq 10\%$ ); Common ( $\geq 1, < 10\%$ ); Uncommon ( $\geq 0.1, < 1\%$ ); Rare ( $\geq 0.01, < 0.1\%$ ); Very rare ( $< 0.01\%$ ), Not known (cannot be established from the available data).

<b>System Organ Class</b>	<b>Very common</b>	<b>Common</b>	<b>Uncommon</b>	<b>Rare</b>
Infections and infestations	Upper respiratory tract infection	Gastroenteritis		
Psychiatric disorders		Anxiety Insomnia Mood alterations with depressive symptoms Depressive disorders Irritability Parasomnias Nervousness Sleep disorders	Panic symptoms Anger Dysphoria Emotional disorder	Hallucinations
Nervous system disorders		Dizziness Memory loss Hypoaesthesia Sciatica	Lethargy	
Vascular disorders		Hot flush		
Respiratory, thoracic and mediastinal disorders			Hiccups	
Gastrointestinal disorders	Nausea	Diarrhoea Vomiting		
Skin and subcutaneous tissue disorders		Pruritus Hyperhidrosis	Night sweats	
Musculoskeletal and connective tissue disorders		Tendonitis Muscle cramp Muscle spasms		
General disorders		Influenza Asthenia/fatigue		
Injury, Poisoning and procedural complications		Joint sprain Contusion Fall		

In clinical studies for other indications, the following additional adverse reactions were commonly reported:

- infections and infestations: sinusitis
- metabolism and nutrition disorders: decreased appetite, anorexia
- nervous system disorders: disturbance in attention
- gastrointestinal disorders: dry mouth, stomach discomfort.

#### **Laboratory adverse events**

ACOMPLIA has not been shown to alter laboratory test values.

#### **4.9 Overdose**

Experience with rimonabant in overdosage is limited. In a single-dose tolerability study, doses up to 300 mg were administered to a limited number of subjects with only minor symptoms reported. These included headache, euphoria, fatigue and insomnia. The pharmacokinetic profile demonstrates that a plateau in exposures is reached at 180 mg. There is no specific antidote for rimonabant; therefore, appropriate supportive measures should be initiated in case of overdose. Treatment should consist of the general measures employed in the management of overdoses, such as keeping airways unobstructed, monitoring cardiovascular function and general symptomatic and supportive measures.

### **5. PHARMACOLOGICAL PROPERTIES**

#### **5.1 Pharmacodynamic properties**

Pharmaco-therapeutic group: {not yet assigned}

ATC code: {not yet assigned }

Rimonabant is a selective cannabinoid-1 receptor (CB1) antagonist that inhibits the pharmacological effects of cannabinoid agonists *in vitro* and *in vivo*.

The endocannabinoid system is a physiological system present in brain and peripheral tissues (including adipocytes) that affects energy balance, glucose and lipid metabolism and body weight, and in neurons of the mesolimbic system modulates the intake of highly palatable, sweet or fatty foods.

#### **Clinical study results**

##### **Weight Management**

In total more than 6800 patients were included in the Phase 2 and Phase 3 clinical studies. The patients included in the phase 3 trials followed a restrictive diet during the trial prescribed by a dietician and they were advised to increase their physical activity. Patients had a BMI  $\leq$  30 kg/m<sup>2</sup> or BMI > 27 kg/m<sup>2</sup> with hypertension and/or dyslipidemia at inclusion. Approximately 80% of the population were women, 87% Caucasian and 9% Black. Experience in patients over 75 years and Orientals/Asians was limited.

Significant mean weight reductions from baseline to one year for ACOMPLIA 20 mg versus placebo were demonstrated in three studies conducted in non-diabetic patients. A mean weight loss of 6.5 kg from baseline to one year was shown for ACOMPLIA 20 mg versus a mean weight loss of 1.6 kg for placebo (Difference -4.9 kg CI<sub>95%</sub> -5.3;-4.4, p< 0.001). In a trial enrolling type 2 diabetics, at one year a mean weight loss of 5.3 kg was shown for ACOMPLIA 20 mg versus a loss on placebo of 1.4 kg (Difference -3.9 kg CI<sub>95%</sub> -4.6;-3.3, p<0.001).

The percentage of patients who lost 5% and 10% of their baseline body weight after 1 year of treatment are given below:

	<b>Non-diabetic studies</b>		<b>Diabetic study</b>	
	<b>Placebo</b>	<b>ACOMPLIA 20 mg</b>	<b>Placebo</b>	<b>ACOMPLIA 20 mg</b>
n <sub>ITT</sub>	1254	2164	348	339
Weight at baseline (kg)	101	101	96	95
Subjects with a 5% weight reduction	19.7%	50.8%	14.5%	49.4%
Difference (CI <sub>95%</sub> )	31.1% (28%; 34%)		34.9% (28%; 41%)	
Subjects with a 10% weight reduction	7.8%	27.0%	2.0%	16.2%
Difference (CI <sub>95%</sub> )	19.2% (17%; 22%)		14.2% (10%; 19%)	

Most of the observed weight reduction was obtained within the first nine months of treatment. ACOMPLIA 20 mg was effective in maintaining weight loss up to two years. Weight loss at two years was 5.1 kg for patients who received ACOMPLIA 20 mg and 1.2 kg for placebo (Difference -3.8 kg; CI<sub>95%</sub> -4.4, -3.3; p<0.001).

Rimonabant 20 mg reduced the risk of weight regain. Patients who received ACOMPLIA 20 mg for one year were re-randomized to ACOMPLIA 20 mg or placebo. At two years, patients continuing on rimonabant had a mean total weight loss of 7.5 kg over 2 years whereas patients re-randomized to placebo group during the second year had a mean total weight loss of 3.1 kg over 2 years. At two years, the difference in total weight loss between ACOMPLIA and placebo was -4.2 kg (CI<sub>95%</sub> -5.0; -3.4, p<0.001).

Treatment with rimonabant was associated with significant reductions in waist circumference, a known marker of intra-abdominal fat.

The effects on body weight appeared to be consistent among men and women. In the limited number of Black patients weight loss was less pronounced (mean difference to placebo -2.9 kg). No conclusions can be drawn with regard to effects in patients over 75 years or in Asian/Oriental patients due to the low number of patients.

#### *Weight management and additional risk factors*

In the non-diabetic studies including a mixed population of subjects with/without (treated) dyslipidemia, an increase in HDL-C and decrease in triglycerides (at one year) was observed. For HDL-C an average increase of 16.4% was seen under rimonabant 20 mg (baseline HDL-C 1.24 mmol/l) compared to an increase of 8.9% for placebo (baseline HDL-C 1.21 mmol/l). The difference was statistically significant (Difference 7.9% CI<sub>95%</sub> 6.6%; 9.2%, p<0.001). For the triglycerides an average decrease of 6.9% was seen under rimonabant 20 mg (baseline TG 1.62 mmol/l) compared to an increase of 5.8% for placebo (baseline TG 1.65 mmol/l). The difference was statistically significant (Difference -13.3% CI<sub>95%</sub> -16.5; -10.2% p<0.001). It is estimated that approximately half of the observed improvement in HDL-C and triglycerides in patients who received rimonabant 20 mg was beyond that expected from weight loss alone.

Generally ACOMPLIA 20 mg had no significant effect on Total-C or LDL-C levels.

In the trial in type 2 diabetic patients who were overweight or obese treated with metformin or sulfonylurea an improvement in HbA1c was observed. The absolute change in HbA1c at one year was -0.6 for rimonabant 20 mg (baseline 7.2%) and +0.1 under placebo (baseline 7.3%). Differences were statistically significant (difference of -0.7%,  $CI_{95\%}$  -0.80;-0.5,  $p<0.001$ ). Changes in HDL-C and TG in this population were similar to that of the non-diabetic population. It is estimated that approximately half of the mean improvement in HbA1c in patients receiving rimonabant 20 mg was beyond that expected from weight loss alone.

## 5.2 Pharmacokinetic properties

Rimonabant pharmacokinetics are fairly dose proportional up to about 20 mg. AUC increased less than in proportion to dose above 20 mg.

### Absorption:

Rimonabant displays high *in vitro* permeability and is not a substrate of P-glycoprotein. The absolute bioavailability of rimonabant has not been determined. Following multiple once-daily doses of 20 mg to healthy subjects in the fasted state, maximum plasma concentrations of rimonabant are achieved in approximately 2 hours with steady state plasma levels achieved within 13 days ( $C_{max} = 196 \pm 28.1$  ng/ml;  $C_{trough} = 91.6 \pm 14.1$  ng/ml;  $AUC_{0-24} = 2960 \pm 268$  ng.h/ml). Steady state rimonabant exposures are 3.3-fold higher than those observed after the first dose. Population pharmacokinetic analysis demonstrated less fluctuation in peak to trough plasma concentration but no differences in steady state AUC as weight increases. As weight increases from 65 to 200 kg,  $C_{max}$  is expected to decrease 24% and  $C_{trough}$  is expected to increase by 5%. Time to steady state is longer in obese patients (25 days) as a consequence of the higher volume of distribution in these patients. Population pharmacokinetic analysis indicated that rimonabant pharmacokinetics are similar between healthy non-smoking subjects and patients who smoke.

### Effect of food:

Administration of rimonabant to healthy subjects in the fasted state or with a high fat meal demonstrated that  $C_{max}$  and AUC were increased 67% and 48% respectively, under fed conditions. In clinical studies, ACOMPLIA 20 mg was taken in the morning usually before breakfast.

### Distribution:

The *in vitro* human plasma protein binding of rimonabant is high (>99.9%) and non-saturable over a wide concentration range. The apparent peripheral volume of distribution of rimonabant appears to be related to body weight, with obese patients having a higher volume of distribution than normal-weight subjects.

### Biotransformation:

Rimonabant is metabolized by both CYP3A and amidohydrolase (predominantly hepatic) pathways *in vitro*. Circulating metabolites do not contribute to its pharmacologic activity.

### Elimination:

Rimonabant is mainly eliminated by metabolism and subsequent biliary excretion of metabolites. Only an approximate 3% of the dose of rimonabant is eliminated in the urine, while approximately 86% of the dose is excreted in the faeces as unchanged drug and metabolites. In obese patients, the elimination half-life is longer (about 16 days) than in non-obese patients (about 9 days) due to a larger volume of distribution.

## Special Populations

### Race:

In single- and repeat-dose studies, the  $C_{max}$  and AUC of rimonabant were similar in healthy Japanese and Caucasian subjects, whereas elimination half-life was shorter in Japanese subjects (3-4 days) compared to Caucasian subjects (about 9 days). The difference in half-life was due to differences in peripheral volume of distribution as a consequence of lower weight in Japanese subjects. Black patients may have up to a 31% lower  $C_{max}$  and a 43% lower AUC than patients of other races.



*Gender:*

The pharmacokinetics of rimonabant are similar in female and male patients.

*Elderly:*

Elderly patients have slightly higher exposure than young patients. Based on a population pharmacokinetic analysis (age range 18 - 81 years) a 75 year old patient is estimated to have a 21% higher  $C_{max}$  and a 27% higher AUC than a 40 year old patient.

*Patients with hepatic insufficiency:*

Mild hepatic impairment does not alter rimonabant exposure. Data are insufficient to draw conclusions regarding pharmacokinetics in moderate hepatic impairment. Patients with severe hepatic impairment were not evaluated.

*Patients with renal impairment:*

The effect of renal function on the pharmacokinetics of rimonabant has not been studied specifically. Based on data from population pharmacokinetic studies, mild and moderate renal impairment do not seem to affect the pharmacokinetics of rimonabant. Limited data suggest an increased exposure in patients with moderate renal impairment (40% increase in AUC). There are no data in severe renal impairment.

### **5.3 Preclinical safety data**

Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:

Convulsions were observed sporadically in studies in rodents and macaques. No convulsions were observed in dogs during a 3 month study. In some, but not all cases, initiation of convulsions appeared to be associated with procedural stress such as handling of the animals. A proconvulsant activity of rimonabant was found in one of two safety pharmacology studies. No adverse effect of rimonabant treatment was observed on EEG patterns in rats.

Increased incidence and/or severity of clinical signs suggestive of increased tactile hyperesthesia were observed in rodent studies. A direct effect of rimonabant cannot be ruled out.

Liver steatosis and a dose-related increase in centrilobular necrosis were observed in long-term studies in the rat. A direct effect of rimonabant cannot be ruled out.

In standard fertility studies in female rats (dosing for 2 weeks prior to mating) there was abnormal oestrous cyclicity and a decrease in corpora lutea and fertility index at doses of rimonabant that induced maternal toxicity (30 and 60 mg/kg/day). Following dosing for a longer treatment duration prior to mating (9 weeks) that permitted recovery from the initial effects of rimonabant, no adverse effects were seen on fertility or oestrous cyclicity. Regarding reproductive parameters, at 30 mg/kg no differences were observed between treated animals and controls, at 60 mg/kg effects were still observed (decreased number of corpora lutea, implantations, total and viable fetuses).

Sporadic malformations (anencephaly, micro-ophthalmia, widened brain ventricles and omphalocele) were observed in the rabbit embryofetal toxicity studies at doses resulting in exposures comparable with the clinical exposures. Although maternal toxicity was observed at these doses, a relation to treatment cannot be excluded. No treatment-related malformations were seen in the rat.

Effects of rimonabant on pre- and post-natal development were assessed in the rat at doses up to 10 mg/kg/day. There was a treatment related increase in pup mortality in the pre-weaning period. The increased pup mortality might be attributable to a failure of the dam to nurse or ingestion of rimonabant in milk and/or inhibition of the suckling reflex that is reported in the literature to be initiated in neonatal mice by endocannabinoid signalling via CB1 receptors. There are reports in the literature that, in both rodents and humans, the spatial distribution and density of CB1 receptors in the brain changes during development. The potential relevance of this to administration of a CB1 antagonist is unknown. In the pre- and post-natal development study in rats, exposure to rimonabant

in utero and via lactation produced no alterations on learning or memory, but equivocal effects on motor activity and auditory startle response were observed in the pups as a result of rimonabant exposure.

## **6. PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

Tablet core:

maize starch,  
lactose monohydrate,  
povidone K 30 (E1201),  
croscarmellose sodium (E468),  
sodium laurilsulfate (E487),  
microcrystalline cellulose (E460),  
magnesium stearate

Tablet coating:

lactose monohydrate,  
hypromellose 15 mPa.s (E464),  
titanium dioxide (E171),  
macrogol 3000

Tablet polishing:

carnauba wax (E903)

### **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-aluminium blister packs containing 14, 28, 56, 84 and 98 film-coated tablets.

70 x 1 film-coated tablets in PVC-aluminium perforated unit dose blister packs.

Opaque white HDPE bottles containing 28, 98 and 500 film-coated tablets.

Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal**

No special requirements

**7. MARKETING AUTHORIZATION HOLDER**

sanofi-aventis.  
174 Avenue de France  
F-75013 Paris  
France

**8. MARKETING AUTHORIZATION NUMBER**

EU/1/06/344/001-009

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

19 June 2006

**10. DATE OF REVISION OF THE TEXT**

**Detailed information on this product is available on the website of the European Medicines Agency (EMA) <http://www.ema.int/>.**

## **ANNEX II**

- A. MANUFACTURING AUTHORISATION HOLDERS  
RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OF THE MARKETING AUTHORISATION**

**A. MANUFACTURING AUTHORISATION HOLDERS RESPONSIBLE FOR BATCH RELEASE**

Name and address of the manufacturers responsible for batch release

Sanofi Winthrop Industrie, 30-36 Avenue Gustave Eiffel, BP 27166, F-37071 Tours Cedex 2, France  
Sanofi-aventis S.p.A., Strada Statale 17, Km 22 , 67019 Scoppito (AQ), Italy

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

**B. CONDITIONS OF THE MARKETING AUTHORISATION**

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to medical prescription.

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable.

- **OTHER CONDITIONS**

The MAH must ensure that the system of pharmacovigilance is in place and functioning before the product is placed on the market.

The MAH commits to performing the studies and additional pharmacovigilance activities detailed in the Pharmacovigilance Plan.

An updated risk management plan should be provided as per the CHMP guideline on risk management systems for medicinal products for human use.

**ANNEX III**  
**LABELLING AND PACKAGE LEAFLET**

## **A. LABELLING**

**PARTICULARS TO APPEAR ON THE OUTER PACKAGING****Carton for the presentations of 14, 28, 56, 70, 84 and 98 film-coated tablets in blisters****1. NAME OF THE MEDICINAL PRODUCT**

ACOMPLIA 20 mg film-coated tablets  
rimonabant

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each tablet contains 20 mg of rimonabant.

**3. LIST OF EXCIPIENTS**

Also contains lactose monohydrate.

See leaflet for further information.

**4. PHARMACEUTICAL FORM AND CONTENTS**

14 film-coated tablets  
28 film-coated tablets  
56 film-coated tablets  
70x1 film coated-tablets  
84 film-coated tablets  
98 film-coated tablets

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Oral use.

Read the package leaflet before use

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

Keep out of the reach and sight of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**



**8. EXPIRY DATE**

EXP {MM/YYYY}

**9. SPECIAL STORAGE CONDITIONS****10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE****11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

sanofi-aventis  
174 avenue de France  
F-75013 Paris  
France

**12. MARKETING AUTHORISATION NUMBER(S)**

EU/1/06/344/001  
EU/1/06/344/002  
EU/1/06/344/003  
EU/1/06/344/004  
EU/1/06/344/005  
EU/1/06/344/006

**13. BATCH NUMBER**

Lot

**14. GENERAL CLASSIFICATION FOR SUPPLY**

Medicinal product subject to medical prescription.

**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

ACOMPLIA

<b>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</b>
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<b>Blisters of the presentations of 14, 28, 56, 84 and 98 film-coated tablets</b>
---

<b>1. NAME OF THE MEDICINAL PRODUCT</b>
---

ACOMPLIA 20 mg film-coated tablets  
rimonabant

<b>2. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
--

sanofi-aventis

<b>3. EXPIRY DATE</b>
-----------------------

EXP {MM/YYYY}

<b>4. BATCH NUMBER</b>
------------------------

Lot

<b>5. OTHER</b>
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Monday  
Tuesday  
Wednesday  
Thursday  
Saturday  
Sunday

<b>MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS</b>
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<b>Blisters of the presentations of 70 x 1 film-coated tablets</b>
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<b>1. NAME OF THE MEDICINAL PRODUCT</b>
---

ACOMPLIA 20 mg film-coated tablets  
rimonabant

<b>2. NAME OF THE MARKETING AUTHORISATION HOLDER</b>
--

sanofi-aventis

<b>3. EXPIRY DATE</b>
-----------------------

EXP {MM/YYYY}

<b>4. BATCH NUMBER</b>
------------------------

Lot

<b>5. OTHER</b>
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**PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND ON THE IMMEDIATE PACKAGING**

**Carton of the presentations of 28, 98 and 500 film-coated tablets in HDPE bottles / HDPE bottle label for the presentations of 28, 98 and 500 film-coated tablets**

**1. NAME OF THE MEDICINAL PRODUCT**

ACOMPLIA 20 mg film-coated tablets  
rimonabant

**2. STATEMENT OF ACTIVE SUBSTANCE(S)**

Each tablet contains 20 mg of rimonabant.

**3. LIST OF EXCIPIENTS**

Also contains lactose monohydrate.

See leaflet for further information.

**4. PHARMACEUTICAL FORM AND CONTENTS**

28 film-coated tablets  
98 film-coated tablets  
500 film-coated tablets

**5. METHOD AND ROUTE(S) OF ADMINISTRATION**

Oral use.  
Read the package leaflet before use.

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

Keep out of the reach and sight of children.

**7. OTHER SPECIAL WARNING(S), IF NECESSARY**

**8. EXPIRY DATE**

EXP {MM/YYYY}

<b>9. SPECIAL STORAGE CONDITIONS</b>
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<b>10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</b>
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<b>11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</b>
---

sanofi-aventis  
174 avenue de France  
F-75013 Paris  
France

<b>12. MARKETING AUTHORISATION NUMBER(S)</b>
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EU/1/06/344/007  
EU/1/06/344/008  
EU/1/06/344/009

<b>13. BATCH NUMBER</b>
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Lot

<b>14. GENERAL CLASSIFICATION FOR SUPPLY</b>
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Medicinal product subject to medical prescription.

<b>15. INSTRUCTIONS ON USE</b>
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<b>16. INFORMATION IN BRAILLE</b>
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ACOMPLIA