ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Xenical 120 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains 120 mg orlistat.

For a full list of excipients, see 6.1.

3. PHARMACEUTICAL FORM

Hard capsule.
The capsule has a turquoise cap and turquoise body bearing the imprint of "XENICAL 120".

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Xenical is indicated in conjunction with a mildly hypocaloric diet for the treatment of obese patients with a body mass index (BMI) greater or equal to 30 kg/m², or overweight patients (BMI $\geq$ 28 kg/m²) with associated risk factors.

Treatment with orlistat should be discontinued after 12 weeks if patients have been unable to lose at least 5 % of the body weight as measured at the start of therapy.

4.2 Posology and method of administration

Adults
The recommended dose of orlistat is one 120 mg capsule taken with water immediately before, during or up to one hour after each main meal. If a meal is missed or contains no fat, the dose of orlistat should be omitted.

The patient should be on a nutritionally balanced, mildly hypocaloric diet that contains approximately 30 % of calories from fat. It is recommended that the diet should be rich in fruit and vegetables. The daily intake of fat, carbohydrate and protein should be distributed over three main meals.

Doses of orlistat above 120 mg three times daily have not been shown to provide additional benefit. The effect of orlistat results in an increase in faecal fat as early as 24 to 48 hours after dosing. Upon discontinuation of therapy, faecal fat content usually returns to pre-treatment levels, within 48 to 72 hours.

Special populations
The effect of orlistat in patients with hepatic and/or renal impairment, children and elderly patients has not been studied.

There is no relevant indication for use of Xenical in children.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Chronic malabsorption syndrome.
- Cholestasis.
- Breast-feeding.

4.4 Special warnings and precautions for use

In clinical trials, the decrease in bodyweight with orlistat treatment was less in type II diabetic patients than in non-diabetic patients. Antidiabetic medicinal product treatment may have to be closely monitored when taking orlistat.

Co-administration of orlistat with ciclosporin is not recommended (see section 4.5).

Patients should be advised to adhere to the dietary recommendations they are given (see section 4.2).

The possibility of experiencing gastrointestinal adverse reactions (see section 4.8) may increase when orlistat is taken with a diet high in fat (e.g. in a 2000 kcal/day diet, > 30 % of calories from fat equates to > 67 g of fat). The daily intake of fat should be distributed over three main meals. If orlistat is taken with a meal very high in fat, the possibility of gastrointestinal adverse reactions may increase.

Cases of rectal bleeding have been reported with Xenical. Prescribers should investigate further in case of severe and/or persistent symptoms.

The use of an additional contraceptive method is recommended to prevent possible failure of oral contraception that could occur in case of severe diarrhoea (see section 4.5).

Coagulation parameters should be monitored in patients treated with concomitant oral anticoagulants (see section 4.5 and 4.8).

The use of orlistat may be associated with hyperoxaluria and oxalate nephropathy leading sometimes to renal failure. This risk is increased in patients with underlying chronic kidney disease and/or volume depletion (see section 4.8).

Rare occurrence of hypothyroidism and/or reduced control of hypothyroidism may occur. The mechanism, although not proven, may involve a decreased absorption of iodine salts and/or levothyroxine (see section 4.5).

Antiepileptics patient: Orlistat may unbalance anticonvulsant treatment by decreasing the absorption of antiepileptic drugs, leading to convulsions (see section 4.5).

Antiretrovirals for HIV: Orlistat may potentially reduce the absorption of antiretroviral medicines for HIV and could negatively affect the efficacy of antiretroviral medications for HIV (see section 4.5).

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Ciclosporin
A decrease in ciclosporin plasma levels has been observed in a drug-drug-interaction study and also reported in several cases, when orlistat was administered concomitantly. This can lead to a decrease of immunosuppressive efficacy. Therefore the combination is not recommended (see section 4.4). However, if such concomitant use is unavoidable, more frequent monitoring of ciclosporin blood levels should be performed both after addition of orlistat and upon discontinuation of orlistat in ciclosporin treated patients. Ciclosporin blood levels should be monitored until stabilised.

Acarbose
In the absence of pharmacokinetic interaction studies, the concomitant administration of orlistat with acarbose should be avoided.

Oral anticoagulants

When warfarin or other anticoagulants are given in combination with orlistat, international normalised ratio (INR) values should be monitored (see section 4.4).

Fat soluble vitamins
Treatment with orlistat may potentially impair the absorption of fat-soluble vitamins (A, D, E and K). The vast majority of patients receiving up to four full years of treatment with orlistat in clinical studies had vitamin A, D, E and K and beta-carotene levels that stayed within normal range. In order to ensure adequate nutrition, patients on a weight control diet should be advised to have a diet rich in fruit and vegetables and use of a multivitamin supplement could be considered. If a multivitamin supplement is recommended, it should be taken at least two hours after the administration of orlistat or at bedtime.

Amiodarone
A slight decrease in plasma levels of amiodarone, when given as a single dose, has been observed in a limited number of healthy volunteers who received orlistat concomitantly. In patients receiving amiodarone treatment, the clinical relevance of this effect remains unknown but may become clinically relevant in some cases. In patients receiving concomitant amiodarone treatment, reinforcement of clinical and ECG monitoring is warranted.

Convulsions have been reported in patients treated concomitantly with orlistat and antiepileptic drugs e.g. valproate, lamotrigine, for which a causal relationship to an interaction cannot be excluded. Therefore, these patients should be monitored for possible changes in the frequency and/or severity of convulsions.

Rare occurrence of hypothyroidism and/or reduced control of hypothyroidism may occur. The mechanism, although not proven, may involve a decreased absorption of iodine salts and/or levothyroxine (see section 4.4).

There are some case reports of reduced efficacy of antiretroviral HIV medicines, antidepressants antipsychotics (including lithium) and benzodiazepines coincidental to the initiation of orlistat treatment in previously well-controlled patients. Therefore orlistat treatment should only be initiated after careful consideration of the possible impact in these patients.

Lack of interactions
No interactions with amitriptyline, atorvastatin, biguanides, digoxin, fibrates, fluoxetine, losartan, phenytoin, phentermine, pravastatin, nifedipine Gastrointestinal Therapeutic System (GITS), nifedipine slow release, sibutramine or alcohol have been observed. The absence of these interactions has been demonstrated in specific drug-drug-interaction studies.

The absence of an interaction between oral contraceptives and orlistat has been demonstrated in specific drug-drug interaction studies. However, orlistat may indirectly reduce the availability of oral contraceptives and lead to unexpected pregnancies in some individual cases. An additional contraceptive method is recommended in case of severe diarrhoea (see section 4.4).

4.6 Fertility, pregnancy and lactation

For orlistat no clinical data on exposed pregnancies are available.
Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see section 5.3).
Caution should be exercised when prescribing to pregnant women.

As it is not known whether orlistat is secreted into human milk, orlistat is contra-indicated during breast-feeding.

4.7 Effects on ability to drive and use machines

Xenical has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions to orlistat are largely gastrointestinal in nature. The incidence of adverse events decreased with prolonged use of orlistat.

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000) and very rare (<1/10,000) including isolated reports.

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

The following table of undesirable effects (first year of treatment) is based on adverse events that occurred at a frequency of > 2 % and with an incidence ≥ 1 % above placebo in clinical trials of 1 and 2 years duration:

System organ class	Adverse reaction/event
Nervous system disorders Very common:	 Headache
Respiratory, thoracic and mediastinal disorders Very common: Common:	 Upper respiratory infection Lower respiratory infection
Gastrointestinal disorders Very common: Common:	 Abdominal pain/discomfort Oily spotting from the rectum Flatus with discharge Faecal urgency Fatty/oily stool Flatulence Liquid stools Oily evacuation Increased defecation Rectal pain/discomfort Soft stools Faecal incontinence Abdominal distension* Tooth disorder Gingival disorder
Renal and urinary disorders Common:	 Urinary tract infection
Metabolism and nutrition disorders Very common:	 Hypoglycemia*
Infections and infestations Very common:	 Influenza
General disorders and administration site conditions Common:	 Fatigue
Reproductive system and breast disorders Common:	 Menstrual irregularity
Psychiatric disorders Common:	 Anxiety

* only unique treatment adverse events that occurred at a frequency of > 2 % and with an incidence ≥ 1 % above placebo in obese type 2 diabetic patients.

In a 4 year clinical trial, the general pattern of adverse event distribution was similar to that reported for the 1 and 2 year studies with the total incidence of gastrointestinal related adverse events occurring in year 1 decreasing year on year over the four year period.

The following table of undesirable effects is based on post-marketing spontaneous reports, and therefore the frequency remains unknown:

System organ class	Adverse reaction
Investigations	Increase in liver transaminases and in alkaline phosphatase. Decreased prothrombin, increased INR and unbalanced anticoagulant treatment resulting in variations of haemostatic parameters have been reported in patients treated with anticoagulants in association with orlistat (see section 4.4 and 4.5)
Gastrointestinal disorders	Rectal bleeding Diverticulitis Pancreatitis
Skin and subcutaneous tissue disorders	Bullous eruptions
Immune system disorders	Hypersensitivity (e.g. pruritus, rash, urticaria, angioedema, bronchospasm and anaphylaxis)
Hepatobiliary disorders	Cholelithiasis Hepatitis that may be serious. Some fatal cases or cases requiring liver transplantation have been reported.
Renal and urinary disorders	Oxalate nephropathy that may lead to renal failure

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V*.

4.9 Overdose

Single doses of 800 mg orlistat and multiple doses of up to 400 mg three times daily for 15 days have been studied in normal weight and obese subjects without significant adverse findings. In addition, doses of 240 mg tid have been administered to obese patients for 6 months. The majority of orlistat overdose cases received during post-marketing reported either no adverse events or adverse events that are similar to those reported with recommended dose.

Should a significant overdose of orlistat occur, it is recommended that the patient be observed for 24 hours. Based on human and animal studies, any systemic effects attributable to the lipase-inhibiting properties of orlistat should be rapidly reversible.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group: Peripherally acting antiobesity agent, ATC code A08AB01.

Orlistat is a potent, specific and long-acting inhibitor of gastrointestinal lipases. It exerts its therapeutic activity in the lumen of the stomach and small intestine by forming a covalent bond with the active serine site of the gastric and pancreatic lipases. The inactivated enzyme is thus unavailable to hydrolyse dietary fat, in the form of triglycerides, into absorbable free fatty acids and monoglycerides.

In the 2-year studies and the 4-year study, a hypocaloric diet was used in association with treatment in both the orlistat and the placebo treated groups.

Pooled data from five 2 year studies with orlistat and a hypocaloric diet showed that 37 % of orlistat patients and 19 % of placebo patients demonstrated a loss of at least 5 % of their baseline body weight after 12 weeks of treatment. Of these, 49 % of orlistat treated patients and 40 % of placebo treated patients went on to lose ≥ 10 % of their baseline body weight at one year. Conversely, of patients failing to demonstrate a loss of 5 % of their baseline body weight after 12 weeks of treatment, only 5 % of orlistat treated patients and 2 % of placebo treated patients went on to lose ≥ 10 % of their baseline body weight at one year. Overall, after one year of treatment, the percentage of patients taking 120 mg orlistat who lost 10 % or more of their body weight was 20 % with orlistat 120 mg compared to 8 % of patients taking placebo. The mean difference in weight loss with the drug compared to placebo was 3.2 kg.

Data from the 4-year XENDOS clinical trial showed that 60 % of orlistat patients and 35 % of placebo patients demonstrated a loss of at least 5 % of their baseline body weight after 12 weeks of treatment. Of these, 62 % of orlistat treated patients and 52 % of placebo treated patients went on to lose ≥ 10 % of their baseline body weight at one year. Conversely, of patients failing to demonstrate a loss of 5 % of their baseline body weight after 12 weeks of treatment, only 5 % of orlistat treated patients and 4 % of placebo treated patients went on to lose ≥ 10 % of their baseline body weight at one year. After 1 year of treatment, 41 % of the orlistat treated patients versus 21 % of placebo treated patients lost ≥ 10 % of body weight with a mean difference of 4.4 kg between the two groups. After 4 years of treatment 21 % of the orlistat treated patients compared to 10 % of the placebo treated patients had lost ≥ 10 % of body weight, with a mean difference of 2.7 kg.

More patients on orlistat or placebo lost baseline body weight of at least 5 % at 12 weeks or 10 % at one year in the XENDOS study than in the five 2-year studies. The reason for this difference is that the five 2-year studies included a 4-week diet and placebo lead-in period during which patients lost on average 2.6 kg prior to commencing treatment.

Data from the 4-year clinical trial also suggested that weight loss achieved with orlistat delayed the development of type 2 diabetes during the study (cumulative diabetes cases incidences: 3.4 % in the orlistat group compared to 5.4 % in the placebo-treated group). The great majority of diabetes cases came from the subgroup of patients with impaired glucose tolerance at baseline, which represented 21 % of the randomised patients. It is not known whether these findings translate into long-term clinical benefits.

In obese type 2 diabetic patients insufficiently controlled by antidiabetic agents, data from four one-year clinical trials showed that the percentage of responders (≥ 10 % of body weight loss) was 11.3 % with orlistat as compared to 4.5 % with placebo. In orlistat-treated patients, the mean difference from placebo in weight loss was 1.83 kg to 3.06 kg and the mean difference from placebo in HbA1c reduction was 0.18 % to 0.55 %. It has not been demonstrated that the effect on HbA1c is independent from weight reduction.

In a multi-centre (US, Canada), parallel-group, double-blind, placebo-controlled study, 539 obese adolescent patients were randomised to receive either 120 mg orlistat (n=357) or placebo (n=182) three times daily as an adjunct to a hypocaloric diet and exercise for 52 weeks. Both populations received multivitamin supplements. The primary endpoint was the change in body mass index (BMI) from baseline to the end of the study.

The results were significantly superior in the orlistat group (difference in BMI of 0.86 kg/m^2 in favour of orlistat). 9.5 % of the orlistat treated patients versus 3.3 % of the placebo treated patients lost ≥ 10 % of body weight after 1 year with a mean difference of 2.6 kg between the two groups. The difference was driven by the outcome in the group of patients with ≥ 5 % weight loss after 12 weeks of treatment with orlistat representing 19 % of the initial population. The side effects were generally similar to those observed in adults. However, there was an unexplained increase in the incidence of bone fractures (6 % versus 2.8 % in the orlistat and placebo groups, respectively).

5.2 Pharmacokinetic properties

Absorption
Studies in normal weight and obese volunteers have shown that the extent of absorption of orlistat was minimal. Plasma concentrations of intact orlistat were non-measurable (< 5 ng/ml) eight hours following oral administration of orlistat.

In general, at therapeutic doses, detection of intact orlistat in plasma was sporadic and concentrations were extremely low (< 10 ng/ml or 0.02 μmol), with no evidence of accumulation, which is consistent with minimal absorption.

Distribution
The volume of distribution cannot be determined because the drug is minimally absorbed and has no defined systemic pharmacokinetics. *In vitro* orlistat is > 99 % bound to plasma proteins (lipoproteins and albumin were the major binding proteins). Orlistat minimally partitions into erythrocytes.

Metabolism
Based on animal data, it is likely that the metabolism of orlistat occurs mainly within the gastrointestinal wall. Based on a study in obese patients, of the minimal fraction of the dose that was absorbed systemically, two major metabolites, M1 (4-member lactone ring hydrolysed) and M3 (M1 with N-formyl leucine moiety cleaved), accounted for approximately 42 % of the total plasma concentration.

M1 and M3 have an open beta-lactone ring and extremely weak lipase inhibitory activity (1000 and 2500 fold less than orlistat respectively). In view of this low inhibitory activity and the low plasma levels at therapeutic doses (average of 26 ng/ml and 108 ng/ml respectively), these metabolites are considered to be pharmacologically inconsequential.

Elimination
Studies in normal weight and obese subjects have shown that faecal excretion of the unabsorbed drug was the major route of elimination. Approximately 97 % of the administered dose was excreted in faeces and 83 % of that as unchanged orlistat.
The cumulative renal excretion of total orlistat-related materials was < 2 % of the given dose. The time to reach complete excretion (faecal plus urinary) was 3 to 5 days. The disposition of orlistat appeared to be similar between normal weight and obese volunteers. Orlistat, M1 and M3 are all subject to biliary excretion.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to reproduction.

In animal reproductive studies, no teratogenic effect was observed. In the absence of a teratogenic effect in animals, no malformative effect is expected in man. To date, active substances responsible for malformations in man have been found teratogenic in animals when well-conducted studies were performed in two species.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule filling:
microcrystalline cellulose (E460)
sodium starch glycolate (type A)
povidone (E1201)
sodium laurilsulfate
talc

Capsule shell:
gelatine
indigo carmine (E132)
titanium dioxide (E171)
edible printing ink (black iron oxide, ammonia solution concentrated, potassium hydroxide, shellac, propylene glycol)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Blisters: Do not store above 25 °C. Store in original package and keep the blister in the outer carton in order to protect from light and moisture.

Bottles: Do not store above 30 °C. Keep the container tightly closed in order to protect from moisture.

6.5 Nature and contents of container

PVC/ PVDC blisters containing 21, 42 and 84 hard capsules.
Glass bottles with desiccant containing 21, 42 and 84 hard capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

CHEPLAPHARM Arzneimittel GmbH
Ziegelhof 24
17489 Greifswald
Germany

8. MARKETING AUTHORISATION NUMBERS

EU/1/98/071/001-006

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 29 July 1998
Date of latest renewal: 17 June 2008

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

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

A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

CHEPLAPHARM Arzneimittel GmbH
Bahnhofstr. 1a
17498 Mesekenhagen
Germany

or

CHEPLAPHARM Arzneimittel GmbH
Ziegelhof 23-24
17489 Greifswald
Germany

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 OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list)) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines webportal.

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

- Risk Management Plan (RMP)

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

An updated RMP should be submitted:

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

If the submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time
.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR BLISTER PACKS

1. NAME OF THE MEDICINAL PRODUCT

Xenical 120 mg hard capsules
Orlistat

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 120 mg orlistat.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

21 hard capsules
42 hard capsules
84 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Read the package leaflet before use

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

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 25 °C
Store in original package and keep the blister in the outer carton in order to protect from light and moisture.

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

CHEPLAPHARM Arzneimittel GmbH
Ziegelhof 24
17489 Greifswald
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/98/071/001 21 capsules
EU/1/98/071/002 42 capsules
EU/1/98/071/003 84 capsules

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

xenical

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOIL

1. NAME OF THE MEDICINAL PRODUCT

Xenical 120 mg hard capsules
Orlistat

2. NAME OF THE MARKETING AUTHORISATION HOLDER

CHEPLAPHARM Arzneimittel GmbH

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

OUTER CARTON AND BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT

Xenical 120 mg hard capsules
Orlistat

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each capsule contains 120 mg orlistat.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

21 hard capsules
42 hard capsules
84 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use

Read the package leaflet before use

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

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Do not store above 30 °C
Keep the container tightly closed in order to protect from moisture

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

CHEPLAPHARM Arzneimittel GmbH
Ziegelhof 24
17489 Greifswald
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/98/071/004 21 capsules
EU/1/98/071/005 42 capsules
EU/1/98/071/006 84 capsules

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

xenical

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Xenical 120mg hard capsules
Orlistat

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, please ask your doctor or your pharmacist.
- 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 of the 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 XENICAL is and what it is used for

Xenical is a medicine used to treat obesity. It works in your digestive system to block about one-third of the fat in the food you eat from being digested.
Xenical attaches to the enzymes in your digestive system (lipases) and blocks them from breaking down some of the fat you have eaten during your meal. The undigested fat cannot be absorbed and is eliminated by your body.

Xenical is indicated in the treatment of obesity in conjunction with a low calorie intake diet.

2. What you need to know before you take XENICAL

Do not take XENICAL
- if you are allergic (hypersensitive) to orlistat or to any of the other ingredients of Xenical,
- if you have chronic malabsorption syndrome (insufficient absorption of nutrients from alimentary tract),
- if you have cholestasis (liver disorder)
- if you are breast-feeding

Warnings and precautions
Weight loss may also affect the dose of medicines taken for other conditions (e.g. high cholesterol or diabetes). Be sure to discuss these and other medicines you may be taking with your doctor. Losing weight may mean you need adjustments to the dose of these medicines.

To gain the maximum benefit from Xenical you should follow the nutrition program recommended to you by your doctor. As with any weight-control program, over-consumption of fat and calories may reduce any weight loss effect.

This medicine can cause harmless changes in your bowel habits, such as fatty or oily stools, due to the elimination of undigested fat in your faeces. The possibility of this happening may increase if Xenical is taken with a diet high in fat. In addition your daily intake of fat should be distributed evenly over three main meals because if Xenical is taken with a meal very high in fat, the possibility of gastrointestinal effects may increase.

The use of an additional contraceptive method is recommended to prevent possible failure of oral contraception that could occur in case of severe diarrhoea.

The use of orlistat may be associated with renal stones in patients suffering from chronic kidney disease. Inform your doctor whether you suffer from problems with your kidney.

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

Children
Xenical is not intended to be used in children.

Other medicines and Xenical
Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed.

This is important as using more than one medicine at the same time can strengthen or weaken the effects of the medicines.

Xenical may modify the activity of

- Anticoagulant drugs (e.g. warfarin). Your doctor may need to monitor your blood coagulation.
- Ciclosporin. Co-administration with ciclosporin is not recommended. Your doctor may need to monitor your ciclosporin blood levels more frequently than usual.
- Iodine salts and/or levothyroxine. Cases of hypothyroidism and/or reduced control of hypothyroidism may occur.
- Amiodarone. You may ask your doctor for advice.
- Medicines to treat HIV.
- Medicines for depression, psychiatric disorders or anxiousness

Xenical reduces the absorption of supplements of some fat soluble nutrients, particularly beta-carotene and vitamin E. You should therefore follow your doctor's advice in taking a well balanced diet rich in fruit and vegetables. Your doctor may suggest you take a multivitamin supplement.

Orlistat may unbalance an anticonvulsant treatment, by decreasing the absorption of antiepileptic drugs, thus leading to convulsions. Please contact your doctor if you think that the frequency and/or severity of the convulsions have changed when taking Xenical together with antiepileptic drugs.

Xenical is not recommended for people taking acarbose (an anti-diabetic drug used to treat type 2 diabetes mellitus).

Xenical with food and drink
Xenical can be taken immediately before, during a meal or up to one hour after a meal. The capsule should be swallowed with water.

Pregnancy and breast-feeding
Taking Xenical during pregnancy is not recommended.
You must not breast-feed your infant during treatment with Xenical as it is not known whether Xenical passes into human milk.

Driving and using machines

Xenical has no known effect on your ability to drive a car or operate machinery.

3. How to take XENICAL

Always take Xenical exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. The usual dose of Xenical is one 120 mg capsule taken with each of the three main meals per day. It can be taken immediately before, during a meal or up to one hour after a meal. The capsule should be swallowed with water.

Xenical should be taken with a well-balanced, calorie controlled diet that is rich in fruit and vegetables and contains an average of 30 % of the calories from fat. Your daily intake of fat, carbohydrate and protein should be distributed over three meals. This means you will usually take one capsule at breakfast time, one capsule at lunch time and one capsule at dinner time. To gain optimal benefit, avoid the intake of food containing fat between meals, such as biscuits, chocolate and savoury snacks.

Xenical only works in the presence of dietary fat. Therefore, if you miss a main meal or if you have a meal containing no fat, Xenical need not be taken.

Tell your doctor if, for any reason, you have not taken your medicine exactly as prescribed. Otherwise, your doctor may think that it was not effective or well tolerated and may change your treatment unnecessarily.

Your doctor will discontinue the treatment with Xenical after 12 weeks if you have not lost at least 5 % of your body weight as measured at the start of treatment with Xenical.

Xenical has been studied in long-term clinical studies of up to 4 years duration.

If you take more XENICAL than you should
If you take more capsules than you have been told to take, or if someone else accidentally takes your medicine, contact a doctor, pharmacist or hospital as you may need medical attention.

If you forget to take XENICAL
If you forget to take your medicine at any time, take it as soon as you remember provided this is within one hour of your last meal, then continue to take it at the usual times. Do not take a double dose. If you have missed several doses, please inform your doctor and follow the advice given to you. Do not change the prescribed dose yourself unless your doctor tells you to.

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

4. Possible side effects

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

Tell your doctor or pharmacist as soon as possible if you do not feel well while you are taking Xenical.

The majority of unwanted effects related to the use of Xenical result from its local action in your digestive system. These symptoms are generally mild, occur at the beginning of treatment and are particularly experienced after meals containing high levels of fat. Normally, these symptoms disappear if you continue treatment and keep to your recommended diet.

Very common side effects (affects more than 1 user in 10)

Headache, abdominal pain/discomfort, urgent or increased need to open the bowels, flatulence (wind) with discharge, oily discharge, oily or fatty stools, liquid stools, low blood sugar levels (experienced by some people with type 2 diabetes).

Common side effects (affects 1 to 10 users in 100)

Rectal pain/discomfort, soft stools, incontinence (stools), bloating (experienced by some people with type 2 diabetes), tooth/gum disorder, irregularity of menstrual cycle, tiredness.

The following side effects have also been reported but their frequency cannot be estimated from the available data:

Allergic reactions. The main symptoms are itching, rash, wheals (slightly elevated, itchy skin patches that are paler or redder than surrounding skin), severe difficulty in breathing, nausea, vomiting and feeling unwell. Skin blistering (including blisters that burst). Diverticulitis. Bleeding from the back passage (rectum). Increases in the levels of some liver enzymes may be found in blood tests. Hepatitis (inflammation of the liver). Symptoms can include yellowing skin and eyes, itching, dark coloured urine, stomach pain and liver tenderness (indicated by pain under the front of the rib cage on your right hand side), sometimes with loss of appetite. Stop Xenical if such symptoms occur and tell your doctor. Gallstones. Pancreatitis (inflammation of the pancreas). Oxalate nephropathy (build up of calcium oxalate which may lead to kidney stones). See Chapter 2, take special care with Xenical. Effects on clotting with anti-coagulants.

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

5. How to store XENICAL

Keep out of the sight and reach of children

Blister packs
Do not use Xenical after the expiry date stated on the carton.
Do not store above 25 °C.
Store in original package and keep the blister in the outer carton in order to protect from light and moisture.

Glass bottles
Do not use Xenical after the expiry date stated on the bottle.
Do not store above 30 °C.
Keep container tightly closed in order to protect from moisture.

Medicines should not be disposed via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. Contents of the pack and other information

What XENICAL contains

- The active substance is orlistat. Each capsule contains 120 mg of orlistat.
- The other ingredients are microcrystalline cellulose (E460), sodium starch glycolate (type A), povidone (E1201), sodium laurilsulfate and talc. The capsule shell consists of gelatine, indigo carmine (E132), titanium dioxide (E171) and edible printing ink.

What XENICAL looks like and contents of the pack

Xenical capsules are turquoise with the imprint “XENICAL 120” and are supplied in blister packs and glass bottles, containing 21, 42 and 84 capsules.
Not all pack sizes may be marketed.

Marketing Authorisation Holder
CHEPLAPHARM Arzneimittel GmbH
Ziegelhof 24
17489 Greifswald
Germany

Manufacturer
CHEPLAPHARM Arzneimittel GmbH
Bahnhofstr. 1a
17498 Mesekenhagen
Germany

or

CHEPLAPHARM Arzneimittel GmbH
Ziegelhof 23-24
17489 Greifswald
Germany

This leaflet was last revised in <{MM/YYYY}> <{month YYYY}>.

Detailed information on this medicine is available on the European Medicines Agency web site:
http://www.ema.europa.eu