ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

alli 60 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains 60 mg orlistat.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule.

The capsule has a dark blue centre band, and a turquoise cap and body bearing the imprint of “alli”.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

alli is indicated for weight loss in adults who are overweight (body mass index, BMI, ≥28 kg/m^2) and should be taken in conjunction with a mildly hypocaloric, lower-fat diet.

4.2 Posology and method of administration

Posology

Adults
The recommended treatment dose is one 60 mg capsule to be taken three times daily. No more than three 60 mg capsules should be taken in 24 hours.

Diet and exercise are important parts of a weight loss programme. It is recommended that a diet and exercise programme is started before beginning treatment with alli.

While taking orlistat, the patient should be on a nutritionally balanced, mildly hypocaloric diet that contains approximately 30% of calories from fat (e.g. in a 2,000 kcal/day diet, this equates to <67 g of fat). The daily intake of fat, carbohydrate and protein should be distributed over three main meals.

The diet and exercise programme should continue to be followed when treatment with alli is stopped.

Treatment should not exceed 6 months.

If patients have been unable to lose weight after 12 weeks of treatment with alli, they should consult their doctor or a pharmacist. It may be necessary to discontinue treatment.

Special populations

Elderly (≥65 years old)
There are limited data on the use of orlistat in the elderly. However, as orlistat is minimally absorbed, no dose adjustment is necessary in the elderly.

Hepatic and renal impairment
The effect of orlistat in individuals with hepatic and/or renal impairment has not been studied (see section 4.4). However, as orlistat is minimally absorbed, no dose adjustment is necessary in individuals with hepatic and/or renal impairment.

Paediatric population
The safety and efficacy of alli in children below 18 years of age has not been established. No data are available.

Method of administration

The capsule should be taken with water immediately before, during or up to 1 hour after each main meal. If a meal is missed or contains no fat, the dose of orlistat should be omitted.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Concurrent treatment with ciclosporin (see section 4.5)

- Chronic malabsorption syndrome
- Cholestasis
- Pregnancy (see section 4.6)
- Breast-feeding (see section 4.6)
- Concurrent treatment with warfarin or other oral anticoagulants (see sections 4.5 and 4.8)

4.4 Special warnings and precautions for use

Gastrointestinal symptoms

Patients should be advised to adhere to the dietary recommendations they are given (see section 4.2). The possibility of experiencing gastrointestinal symptoms (see section 4.8) may increase when orlistat is taken with an individual meal or a diet high in fat.

Fat-soluble vitamins

Treatment with orlistat may potentially impair the absorption of fat-soluble vitamins (A, D, E and K) (see section 4.5). For this reason, a multivitamin supplement should be taken at bedtime.

Antidiabetic medicinal products

As weight loss may be accompanied by improved metabolic control in diabetes, patients who are taking a medicinal product for diabetes should consult a doctor before starting treatment with alli, in case it is necessary to adjust the dose of the antidiabetic medicinal product.

Medicinal products for hypertension or hypercholesterolaemia

Weight loss may be accompanied by an improvement in blood pressure and cholesterol levels. Patients who are taking a medicinal product for hypertension or hypercholesterolaemia should consult a doctor or pharmacist when taking alli, in case it is necessary to adjust the dose of these medicinal products.

Amiodarone

Patients who are taking amiodarone should consult a doctor before starting treatment with alli (see section 4.5).

Rectal bleeding

Cases of rectal bleeding have been reported in patients taking orlistat. If this occurs, the patient should consult a doctor.

Oral contraceptives

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).

Kidney disease

Patients with kidney disease should consult a doctor before starting treatment with alli, as 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.

Levothyroxine

Hypothyroidism and/or reduced control of hypothyroidism may occur when orlistat and levothyroxine are co-administered (see section 4.5). Patients taking levothyroxine should consult a doctor before starting treatment with alli, as orlistat and levothyroxine may need to be taken at different times and the dose of levothyroxine may need to be adjusted.

Antiepileptic medicinal products

Patients taking an antiepileptic medicinal product should consult a doctor before starting treatment with alli, as they should be monitored for possible changes in the frequency and severity of convulsions. If this occurs, consideration could be given to administering orlistat and antiepileptic medicinal products at different times (see section 4.5).

Antiretrovirals for HIV

Patients should consult a physician before taking alli concomitantly with antiretroviral medicinal products. Orlistat may potentially reduce the absorption of antiretroviral medicinal products for HIV and could negatively affect the efficacy of antiretroviral medicinal products for HIV (see section 4.5).

Information concerning excipients

alli 60 mg hard capsules contain 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 could potentially lead to a decrease of immunosuppressive efficacy. Concurrent use of alli and ciclosporin is contraindicated (see section 4.3).

Oral anticoagulants

When warfarin or other oral anticoagulants are given in combination with orlistat, international normalised ratio (INR) values could be affected (see section 4.8). Concurrent use of alli and warfarin or other oral anticoagulants is contraindicated (see section 4.3).

Oral contraceptives

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).

Levothyroxine

Hypothyroidism and/or reduced control of hypothyroidism may occur when orlistat and levothyroxine are taken at the same time (see section 4.4). This could be due to a decreased absorption of iodine salts and/or levothyroxine.

Antiepileptic medicinal products

Convulsions have been reported in patients treated concomitantly with orlistat and antiepileptic medicinal products e.g. valproate, lamotrigine, for which a causal relationship to an interaction cannot be excluded. Orlistat may decrease the absorption of antiepileptic medicinal products, leading to convulsions.

Antiretroviral medicinal products

Based on reports from literature and post-marketing experience orlistat may potentially reduce the absorption of antiretroviral medicinal products for HIV and could negatively affect the efficacy of antiretroviral medicinal product for HIV (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 subjects receiving up to 4 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. However, patients should be advised to use a multivitamin supplement at bedtime to help ensure adequate vitamin intake (see section 4.4).

Acarbose

In the absence of pharmacokinetic interaction studies, alli is not recommended to be used by patients receiving acarbose.

Amiodarone

A 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. The clinical relevance of this effect in patients receiving amiodarone treatment remains unknown. Patients who are taking amiodarone should consult a doctor before starting treatment with alli. The dose of amiodarone may need to be adjusted during treatment with alli.

Antidepressants, antipsychotics (including lithium) and benzodiazepines

There are some case reports of reduced efficacy of 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.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / Contraception in males and females
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 sections 4.4 and 4.5).

Pregnancy
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).

alli is contraindicated in pregnancy (see section 4.3).

Breast-feeding
As it is not known whether orlistat is secreted into human milk, alli is contraindicated during breast-feeding (see section 4.3).

Fertility
Animal studies do not indicate harmful effects with respect to fertility.

4.7 Effects on ability to drive and use machines

Orlistat has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

Adverse reactions to orlistat are largely gastrointestinal in nature and related to the pharmacologic effect of the medicinal product on preventing the absorption of ingested fat.

The gastrointestinal adverse reactions identified from clinical trials with orlistat 60 mg of 18 months to 2 years duration were generally mild and transient. They generally occurred early in treatment (within 3 months) and most patients experienced only one episode. Consumption of a diet low in fat will decrease the likelihood of experiencing adverse gastrointestinal reactions (see section 4.4).

Tabulated list of adverse reactions

Adverse reactions 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), very rare (<1/10,000) and not known (cannot be estimated from the available data).

The frequencies of adverse reactions identified during post-marketing use of orlistat are not known as these reactions were reported voluntarily from a population of uncertain size.

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System organ class and frequency	**Adverse reaction**
Blood and lymphatic system disorders *Not known*	 Decreased prothrombin and increased INR (see sections 4.3 and 4.5)
Immune system disorders *Not known*	 Hypersensitivity reactions including anaphylaxis, bronchospasm, angioedema, pruritus, rash, and urticaria
Psychiatric disorders *Common*	 Anxiety†

System organ class and frequency	Adverse reaction
Gastrointestinal disorders *Very common* *Common* *Not known*	 Oily spotting Flatus with discharge Faecal urgency Fatty oily stool Oily evacuation Flatulence Soft stools Abdominal pain Faecal incontinence Liquid stools Increased defaecation Diverticulitis Pancreatitis Mild rectal bleeding (see section 4.4)
Renal and urinary disorders *Not known*	 Oxalate nephropathy that may lead to renal failure
Hepatobiliary disorders *Not known*	 Hepatitis that may be serious. Some fatal cases or cases requiring liver transplantation have been reported. Cholelithiasis Increase in transaminases and in alkaline phosphatase
Skin and subcutaneous tissue disorders *Not known*	 Bullous eruption

†It is plausible that treatment with orlistat can lead to anxiety in anticipation of or secondary to gastrointestinal adverse reactions.

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 clinical findings. In addition, doses of 240 mg three times daily have been administered to obese patients for 6 months. The majority of orlistat overdose cases received during post-marketing reported either no adverse reactions or adverse reactions that are similar to those reported with recommended doses of orlistat.

In the event of an overdose, medical advice should be sought. 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

Pharmacotherapeutic group: antiobesity preparations, excl. diet products, peripherally acting antiobesity products, 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. From clinical studies, it has been estimated that orlistat 60 mg taken three times daily blocks the absorption of approximately 25% of dietary fat. 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 returns to pre-treatment levels, usually within 48 to 72 hours.

Two double-blind, randomised, placebo-controlled studies in adults with a BMI ≥28 kg/m^2 support the efficacy of orlistat 60 mg taken three times daily in conjunction with a hypocaloric, lower-fat diet. The primary parameter, change in body weight from baseline (time of randomisation), was assessed for body weight over time (Table 1) and the percentage of

subjects who lost ≥5% or ≥10% of body weight (Table 2). Although weight loss was assessed during 12 months of treatment in both studies, most weight loss occurred within the first 6 months.

Table 1: Effect of 6 months treatment on body weight measured at baseline				
	Treatment group	**N**	**Relative mean change (%)**	**Mean change (kg)**
Study 1	Placebo	204	-3.24	-3.11
	Orlistat 60 mg	216	-5.55	-5.20 [a]
Study 2	Placebo	183	-1.17	-1.05
	Orlistat 60 mg	191	-3.66	-3.59 [a]
Pooled data	Placebo	387	-2.20	-2.09
	Orlistat 60 mg	407	-4.60	-4.40 [a]
[a] $p<0.001$ versus placebo				

Table 2: Responder analysis at 6 months				
	Lost ≥5% of baseline body weight (%)		**Lost ≥10% of baseline body weight (%)**	
	Placebo	Orlistat 60 mg	Placebo	Orlistat 60 mg
Study 1	30.9	54.6 [a]	10.3	21.3 [b]
Study 2	21.3	37.7 [a]	2.2	10.5 [b]
Pooled data	26.4	46.7 [a]	6.5	16.2 [a]
Comparison versus placebo: [a] $p<0.001$; [b] $p<0.01$				

The weight loss induced by orlistat 60 mg conferred other important health benefits after 6 months of treatment in addition to weight loss. The mean relative change in total cholesterol was -2.4% for orlistat 60 mg (baseline 5.20 mmol/l) and +2.8% for placebo (baseline 5.26 mmol/l). The mean relative change in LDL cholesterol was -3.5% for orlistat 60 mg (baseline 3.30 mmol/l) and +3.8% for placebo (baseline 3.41 mmol/l). For waist circumference, the mean change was -4.5 cm for orlistat 60 mg (baseline 103.7 cm) and -3.6 cm for placebo (baseline 103.5 cm). All comparisons against placebo were statistically significant.

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) 8 hours following oral administration of orlistat 360 mg.

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 active substance 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.

Biotransformation
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 (1,000- and 2,500-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 active substance 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

Nonclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, and toxicity to fertility, reproduction and development.
The medicinal use of orlistat is unlikely to represent a risk to the aquatic or terrestrial environment. However, any possible risk should be avoided (see section 6.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content
Microcrystalline cellulose (E460)
Sodium starch glycolate (Type A)
Povidone (E1201) (K-value 30)
Sodium laurilsulfate
Talc

Capsule shell
Gelatin
Indigo carmine (E132)
Titanium dioxide (E171)
Sodium laurilsulfate
Sorbitan monolaurate

Printing ink
Shellac
Iron oxide black (E172)
Propylene glycol

Capsule band
Gelatin
Polysorbate 80
Indigo carmine (E132)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years.

6.4 Special precautions for storage

Do not store above 25°C.
Keep the container tightly closed in order to protect from moisture.

6.5 Nature and contents of container

High-density polyethylene (HDPE) bottle with child resistant closure containing 42, 60, 84, 90 or 120 hard capsules. The bottle also contains two sealed canisters containing silica gel desiccant.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Haleon Ireland Dungarvan Limited,
Knockbrack,
Dungarvan,
Co. Waterford,
Ireland.

8. MARKETING AUTHORISATION NUMBERS

EU/1/07/401/007-011

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 23 July 2007
Date of latest renewal: 29 June 2017

10. DATE OF REVISION OF THE TEXT

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

ANNEX II

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

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

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

alli 60 mg hard capsules:
Haleon Germany GmbH, Barthstraße 4, 80339 München, Germany
Famar S.A., 48 KM Athens-Lamia, 190 11 Avlona, Greece

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

alli 60 mg hard capsules: Medicinal product not subject to medical prescription.

C. OTHER CONDITIONS AND REQUIRMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

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

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

- **Risk management plan (RMP)**

The marketing authorisation holder (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 lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

alli 60 mg hard capsules
orlistat

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 60 mg orlistat.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

This pack includes:

1 bottle containing 42 hard capsules
1 bottle containing 60 hard capsules
1 bottle containing 84 hard capsules
1 bottle containing 90 hard capsules
1 bottle containing 120 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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.
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

Haleon Ireland Dungarvan Limited,
Knockbrack,
Dungarvan,

Co. Waterford,
Ireland.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/401/007-011

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

For adults with a BMI of 28 or above

Weight loss aid
Can help you lose more weight than dieting alone.

alli is used for weight loss alongside reduced calorie, lower-fat meals in overweight (BMI 28 or above) adults, aged 18 or over.

alli is clinically proven to help you lose more weight than dieting alone. The capsules work only in your digestive system to stop about a quarter of the fat in your meals from being absorbed. This fat passes out of your body and may cause changes to your bowel movements. Eat lower-fat meals to help manage these effects.

To see if your BMI is 28 or above, find your height on the chart. If you weigh less than the weight shown for your height, your BMI is below 28 do not use alli.

Height	**Weight**		**Height**	**Weight**
1.50 m	63 kg		4' 10"	9 st 8 lbs
1.55 m	67.25 kg		5' 0"	10 st 3 lbs
1.60 m	71.75 kg		5' 2"	10 st 13 lbs
1.65 m	76.25 kg		5' 4"	11 st 9 lbs
1.70 m	81 kg		5' 6"	12 st 5 lbs
1.75 m	85.75 kg		5' 8"	13 st 2 lbs
1.80 m	90.75 kg		5' 10"	13 st 13 lbs
1.85 m	95.75 kg		6' 0"	14 st 10 lbs
1.90 m	101 kg		6' 2"	15 st 8 lbs

Being overweight increases your risk of developing several serious health problems such as diabetes and heart disease. You should see your doctor for a check up.

Do not use

- if you are under 18 years old.
- if you are pregnant or breast-feeding.
- if you are taking ciclosporin.
- if you are taking warfarin or any other medicines used to thin the blood.
- if you are allergic to orlistat or any of the ingredients.
- if you have cholestasis (condition where the flow of bile from the liver is blocked).
- if you have problems absorbing food (chronic malabsorption syndrome).

Talk to your doctor before taking alli

- if you are taking amiodarone for heart rhythm problems.
- if you are taking a medicine for diabetes.
- if you are taking a medicine for epilepsy.

- if you have kidney disease.
- if you are taking a thyroid medicine (levothyroxine).
- if you are taking medicines for HIV.

Talk to your doctor or pharmacist when taking alli

- if you are taking a medicine for high blood pressure.
- if you are taking a medicine for high cholesterol.

How to use

- take one capsule whole with water, three times a day with each main meal containing fat.
- do not take more than three capsules a day.
- you should take a multivitamin (containing vitamins A, D, E and K) once a day, at bedtime.
- you should not take alli for more than six months.

16. INFORMATION IN BRAILLE

alli 60 mg hard capsules

17. UNIQUE IDENTIFIER – 2D BARCODE

Not applicable.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

Not applicable.

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT

alli 60 mg hard capsules
orlistat

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 60 mg orlistat.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

42 hard capsules
60 hard capsules
84 hard capsules
90 hard capsules
120 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

Oral 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.
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

Haleon Ireland Dungarvan Limited,
Knockbrack,
Dungarvan,
Co. Waterford,
Ireland.

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/07/401/007-011

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product not subject to medical prescription.

15. INSTRUCTIONS ON USE

Weight loss aid

Adults, aged 18 or over, who are overweight.

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

B. PACKAGE LEAFLET

Package leaflet: Information for the user

alli 60 mg hard capsules
orlistat

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist has told you.
- Keep this leaflet. You may need to read it again.
- Ask your doctor or pharmacist if you need more information or advice.
- 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.
- You must talk to your doctor or pharmacist if you do not lose weight after taking alli for 12 weeks. You may need to stop taking alli.

What is in this leaflet

1. What alli is and what it is used for

alli 60 mg hard capsules (orlistat) is a peripherally acting antiobesity product which is used for weight loss in adults aged 18 and over who are overweight, and have a body mass index (BMI) of 28 or above. alli should be used along with a reduced calorie, lower-fat diet.

BMI is a way to find out if you have a healthy weight, or are overweight, for your height. The chart below will help you find out whether you are overweight and whether alli is right for you.

Find your height on the chart. If you weigh less than the weight shown for your height, do not take alli.

Height	Weight		Height	Weight

1.50 m	63 kg		4' 10"	9 st 8 lbs
1.55 m	67.25 kg		5' 0"	10 st 3 lbs
1.60 m	71.75 kg		5' 2"	10 st 13 lbs
1.65 m	76.25 kg		5' 4"	11 st 9 lbs
1.70 m	81 kg		5' 6"	12 st 5 lbs
1.75 m	85.75 kg		5' 8"	13 st 2 lbs
1.80 m	90.75 kg		5' 10"	13 st 13 lbs
1.85 m	95.75 kg		6' 0"	14 st 10 lbs
1.90 m	101 kg		6' 2"	15 st 8 lbs

Risk of being overweight

Being overweight increases your risk of developing several serious health problems such as diabetes and heart disease. These conditions may not cause you to feel unwell so you should see your doctor for a general health check.

How alli works

The active substance (orlistat) in alli is designed to target fat in your digestive system. It stops about a quarter of the fat in your meals from being absorbed. This fat will pass out of the body in your stools (see section 4). It is therefore important that you commit to a lower-fat diet to manage these effects. If you do, the action of the capsules will assist your efforts by helping you to lose more weight compared to dieting alone. For every 2 kg (4 lb) you lose from dieting alone, alli might help you lose up to 1 kg (2 lb) more.

2. What you need to know before you take alli

Do not take alli
If you are allergic to orlistat or any of the other ingredients of this medicine (listed in section 6).
- If you are pregnant or breast-feeding.
- If you are taking ciclosporin, used after organ transplants, for severe rheumatoid arthritis and some severe skin conditions.
- If you are taking warfarin or other medicines used to thin the blood.
- If you have cholestasis (condition where the flow of bile from the liver is blocked).
- If you have problems absorbing food (chronic malabsorption syndrome) diagnosed by a doctor.

Warning and precautions

Talk to your doctor or pharmacist before taking alli.

- If you have diabetes. Tell your doctor who may need to adjust your anti-diabetic medicine.

- If you have kidney disease. Talk to your doctor before taking alli if you have problems with your kidneys. The use of orlistat may be associated with kidney stones in patients suffering from chronic kidney disease.

Children and adolescents

This medicine must not be taken by children and adolescents under 18 years old.

Other medicines and alli

alli may affect some medicines you have to take.
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Do not take alli with these medicines
- Ciclosporin: ciclosporin is used after organ transplants, for severe rheumatoid arthritis and some severe skin conditions.
- Warfarin or other medicines used to thin the blood.

The oral contraceptive pill and alli
- The oral contraceptive pill may be less effective if you get severe diarrhoea. Use an extra method of contraception if you get severe diarrhoea.

Take a multivitamin every day if you are taking alli
- alli can lower the levels of some vitamins absorbed by your body. The multivitamin should contain vitamins A, D, E and K. You should take the multivitamin at bedtime, when you will not be taking alli, to help ensure that the vitamins are absorbed.

Talk to your doctor before taking alli if you are taking
- amiodarone, used for heart rhythm problems.
- acarbose, (an anti-diabetic medicine used to treat type 2 diabetes mellitus). alli is not recommended for people taking acarbose.
- a thyroid medicine (levothyroxine) as it may be necessary to adjust your dose and take your medicines at different times of the day.
- a medicine for epilepsy as any changes in the frequency and severity of your convulsions should be discussed with your doctor.
- medicines to treat HIV. It is important that you consult your doctor before taking alli if you are receiving treatment for HIV.
- medicines for depression, psychiatric disorders or anxiousness.

Talk to your doctor or pharmacist when taking alli
- If you are taking a medicine for high blood pressure as it may be necessary to adjust your dose.
- If you are taking a medicine for high cholesterol as it may be necessary to adjust your dose.

alli with food and drink

alli should be used along with a reduced calorie, lower-fat diet. Try to start this diet before beginning treatment. For information on how to set your calorie and fat targets, see *Further helpful information* in section 6.

alli can be taken immediately before, during a meal or up to one hour after a meal. The capsule should be swallowed with water. This usually means one capsule at breakfast, lunch and dinner. If you miss a meal, or your meal contains no fat, do not take a capsule. alli does not work unless there is some fat in the meal.

If you eat a high-fat meal, do not take more than the recommended dose. Taking the capsule with a meal containing too much fat may increase your chance of getting diet-related treatment effects (see section 4). Make every effort to avoid any high-fat meals while taking alli.

Pregnancy and breast-feeding

Do not take alli if you are pregnant or breast-feeding

Driving and using machines

alli is unlikely to affect your ability to drive and use machines.

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

3. How to take alli

Preparing to lose weight

1. Choose your start date

Choose the day you will start taking the capsules ahead of time. Before you start taking the capsules, begin your reduced calorie, lower-fat diet and give your body a few days to adjust to your new eating habits. Keep a record of what you are eating in a food diary. Food diaries are effective, because they make you aware of what you are eating, how much you eat, and give you the basis to make changes.

2. Decide on your weight loss goal

Think about how much weight you want to lose and then set a target weight. A realistic goal is to lose between 5% to 10% of your starting weight. The amount of weight you lose may vary from week to week. You should aim to lose weight at a gradual, steady pace of about 0.5 kg (1 lb) per week.

3. Set your calorie and fat targets

To help you reach your weight-loss goal you need to set two daily targets, one for calories and one for fat. For further advice see *Further helpful information* in section 6.

Taking alli

Adults 18 and over
- Take one capsule, three times a day.
- Take alli just before, during or up to one hour after meals. This usually means one capsule at breakfast, lunch and dinner. Make sure your three main meals are well balanced, reduced calorie, and lower-fat.

- If you miss a meal, or your meal contains no fat, do not take a capsule. alli does not work unless there is some fat in the meal.
- Swallow the capsule whole with water.
- Do not take more than 3 capsules a day.
- Eat lower-fat meals to reduce the chance of diet-related treatment effects (see section 4).
- Try to be more physically active before you start taking the capsules. Physical activity is an important part of a weight loss programme. Remember to check with your doctor first if you have not exercised before.
- Continue to be active while taking alli and after you stop taking it.

How long should I take alli for?

- alli should not be taken for more than six months.
- If you do not lose weight after taking alli for 12 weeks, see your doctor or pharmacist for advice. You may need to stop taking alli.
- Successful weight loss is not just about eating differently for a short period of time before reverting to your old habits. People who lose weight and maintain the loss make lifestyle changes, which include changes to what they eat and how active they are.

If you take more alli than you should

Do not take more than 3 capsules a day.

➔ If you have taken too many capsules, contact a doctor as soon as possible.

If you forget to take alli

If you miss taking a capsule:

- If it is less than an hour since your last main meal, take the missed capsule.
- If it is more than an hour since your last main meal, do not take the missed capsule. Wait and take the next capsule around your next main meal as usual.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Most of the common side effects related to alli (for example, wind with or without oily spotting, sudden or more frequent bowel motions and soft stools) are caused by the way it works (see section 1). Eat lower-fat meals to help manage these diet-related treatment effects.

Serious side effects
It is not known how frequently these side effects occur

Severe allergic reactions
- Signs of a severe allergic reaction include: severe breathing difficulties, sweating, rash, itching, swollen face, rapid heart beat, collapse.

➔ Stop taking the capsules. Get medical help immediately.

Other serious side effects
- Bleeding from the back passage (rectum)
- Diverticulitis (inflammation of the large intestine). Symptoms may include lower stomach (abdominal) pain, particularly on the left side, possibly with fever and constipation
- Pancreatitis (inflammation of the pancreas). Symptoms may include severe abdominal pain sometimes radiating towards the back, possibly with fever, nausea and vomiting
- Skin blistering (including blisters that burst)
- Severe stomach pain caused by gallstones.
- 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.
- Oxalate nephropathy (build up of calcium oxalate which may lead to kidney stones). See section 2, warnings and precautions.

➔ Stop taking the capsules. Tell your doctor if you get any of these.

Very common side effects
These may affect more than 1 in 10 people
- Wind (flatulence), with or without oily spotting
- Sudden bowel motions
- Fatty or oily stools
- Soft stools

➔ Tell your doctor or pharmacist if any of these side effects gets severe or troublesome.

Common side effects
These may affect up to 1 in 10 people
- Stomach (abdominal) pain
- Incontinence (stools)
- Runny/liquid stools
- More frequent bowel motions
- Anxiety

➔ Tell your doctor or pharmacist if any of these side effects gets severe or troublesome.

Effects seen in blood tests
It is not known how frequently these effects occur (frequency cannot be estimated from the available data)
- Increases in the levels of some liver enzymes
- Effects on blood clotting in people taking warfarin or other blood-thinning (anti-coagulant) medicines

➔ Tell your doctor that you are taking alli when you have a blood test.

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.

Learn to deal with alli effects related to your diet or fat intake

The most common side effects are caused by the way the capsules work and result from some of the fat being passed out of your body. Such effects typically occur within the first few weeks of using the capsules, before you may have learnt to limit the amount of fat in your diet. Such diet-related treatment effects may be a signal that you have eaten more fat than you should have done.

You can learn to minimise the impact of diet-related treatment effects by following these guidelines:
- Start your lower-fat diet a few days, or even a week, before you begin taking the capsules.
- Find out more about how much fat your favourite foods typically contain, and the size of your portions. By familiarising yourself with portions you will be less likely to accidentally exceed your fat target.
- Distribute your fat allowance evenly across your meals for the day. Do not “save up” fat and calorie allowances and then splurge on a high-fat meal or dessert, as you may have done on other weight loss programmes.
- Most users who experience these effects find that they can manage and control them by adjusting their diet.

Do not be concerned if you do not experience any of these problems. This does not mean that the capsules are not working.

5. How to store alli

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the carton and bottle after “EXP”. The expiry date refers to the last day of that month.
- Do not store above 25°C.
- Keep the container tightly closed to protect from moisture.
- The bottle contains two sealed canisters containing silica gel to keep the capsules dry. Keep the canisters in the bottle. Do not swallow them.
- 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 alli contains

The active substance is orlistat. Each hard capsule contains 60 mg of orlistat.
The other ingredients are:
- Capsule filling: microcrystalline cellulose (E460), sodium starch glycolate, povidone (E1201), sodium laurilsulfate, talc.
- Capsule shell: gelatin, indigo carmine (E132), titanium dioxide (E171), sodium laurilsulfate, sorbitan monolaurate, black ink (shellac, iron oxide black (E172), propylene glycol).
- Capsule band: gelatin, polysorbate 80, indigo carmine (E132).

What alli looks like and contents of the pack

alli capsules have a turquoise cap and body, with a dark blue band round the middle, imprinted with "alli".

alli is available in pack sizes of 42, 60, 84, 90 and 120 capsules. Not all pack sizes may be available in all countries.

Marketing Authorisation Holder

Haleon Ireland Dungarvan Limited, Knockbrack, Dungarvan, Co. Waterford,
Ireland

Manufacturer
Haleon Germany GmbH, Barthstraße 4, 80339 München, Germany
Famar S.A, 48 KM Athens-Lamia,
190 11 Avlona, Greece

This leaflet was last revised in November 2024.

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

FURTHER HELPFUL INFORMATION

Risk of being overweight

Being overweight will affect your health and increase your risk of developing serious health problems such as:
- High blood pressure
- Diabetes
- Heart disease
- Stroke
- Certain forms of cancer
- Osteoarthritis

Talk to your doctor about your risk of developing these conditions.

Importance of losing weight

Losing weight and maintaining weight loss, for example by improving your diet and increasing your physical activity, can help reduce the risk of serious health problems and help improve your health.

Helpful tips on your diet and your calorie and fat targets while taking alli

alli should be used along with a reduced calorie, lower-fat diet. The capsules work by preventing some of the fat you eat from being absorbed but you can still eat foods from all the main food groups. Although you should focus on the calories and fat that you eat, it is important to eat a balanced diet. You should choose meals which contain a range of different nutrients and learn to eat healthily for the long term.

Understanding the importance of calorie and fat targets

Calories are a measurement of the energy your body needs. They are sometimes called kilocalories or kcal. Energy may also be measured in kilojoules, which you may also see on food labels.
- The calorie target is the maximum number of calories you will eat each day. See the chart further on in this section.
- Your fat gram target is the maximum number of grams of fat you will eat in each meal. The fat gram target chart follows the information below on setting your calorie target.
- Controlling your fat target is essential because of the way the capsules work. Taking alli means your body will pass more fat through, and therefore may struggle to cope with eating as much fat as before. So by meeting your fat target, you will maximise weight loss results while minimising the risk of diet-related treatment effects.
- You should aim to lose weight gradually and steadily. Losing around 0.5 kg (1 lb) per week is ideal.

How to set your calorie target

The following table has been worked out so that it gives you a calorie target that is about 500 calories fewer per day than your body needs to maintain your current weight. That adds up to 3500 fewer calories per week, about the number of calories in 0.5 kg (1 lb) of fat.

Your calorie target alone should allow you to lose weight at a gradual, steady pace of about 0.5 kg (1 lb) per week, without feeling frustrated or deprived.

Eating fewer than 1200 calories per day is not recommended.

You will need to know your activity level to set your calorie targets. The more active you are, the higher your calorie target.
- Low activity means you do little or no walking, climbing stairs, gardening, or other physical activity on a daily basis.
- Moderate activity means you burn around 150 calories per day in physical activity, for example, walking three kilometres (2 miles), gardening for 30 to 45 minutes, or running two kilometres (1.25 miles) in 15 minutes. Choose the level that most closely fits your daily routine. If you are unsure which level you are, choose Low activity.

Women

Low activity	Below 68.1 kg	Below 10 st 10 lb	1200 calories
	68.1 kg to 74.7 kg	10 st 10 lb to 11 st 11 lb	1400 calories
	74.8 kg to 83.9 kg	11 st 12 lb to 13 st 2 lb	1600 calories
	84.0 kg and over	13 st 3 lb and over	1800 calories
Moderate activity	Below 61.2 kg	Below 9 st 9 lb	1400 calories
	61.3 kg to 65.7 kg	9 st 9 lb to 10 st 4 lb	1600 calories
	65.8 kg and over	10 st 5 lb and over	1800 calories

Men

Low activity	Below 65.7 kg	Below 10 st 4 lb	1400 calories
	65.8 kg to 70.2 kg	10 st 5 lb to 11 st	1600 calories
	70.3 kg and over	11 st 1 lb and over	1800 calories
Moderate activity	59.0 kg and over	9 st 4 lb and over	1800 calories

How to set your fat target

The following chart shows how to set your fat target based on the amount of calories you are allowed per day. You should plan to have three meals per day. If you have set a target of 1400 calories per day, for example, the maximum amount of fat allowed per meal would be 15 g. To stay within your daily allowance for fat, snacks should contain no more than 3 g of fat.

Amount of calories you can eat per day	**Maximum amount of fat allowed per meal**	**Maximum amount of fat allowed from snacks per day**
1200	12 g	3 g
1400	15 g	3 g
1600	17 g	3 g
1800	19 g	3 g

Remember

- Stick to realistic calorie and fat targets as this is a good way of maintaining your weight loss achievements in the long-term.
- Write down what you eat in a food diary, including the calorie and fat content.
- Try to be more physically active before you start taking the capsules. Physical activity is an important part of a weight loss programme. Remember to check with your doctor first if you have not exercised before.
- Continue to be active while taking alli and after you stop taking it.

The alli weight loss programme combines the capsules with an eating plan and a wide range of resources to help you understand how to eat a reduced calorie, lower-fat diet and guidelines for becoming more active.