

ANNEX I

Substance: Clobenzorex

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Spain	Instituto Llorente SA Crta. Del Pardo, Km 1 Madrid ES 28035 Spain	Finedal
France	Laboratoires Diamant Tour Roussel Hoechst Paris La Defense Cedex 3 FR 92080 France	Dinintel
Portugal	Roussel Portugal Lda Rua Joào de Deus, 19-Venda Nova Venda Nova Amadora Codex PT 2701 Portugal	Dinintel

Substance: Norpseudoephedrine

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Germany	Apotheker Dieter Funcke Bahnhofstrasse 64 Oberhausen DE 46145 Germany	Fasupond
Germany	Haenseler GmbH Gottlieb - Daimler - Strasse 1 Konstanz DE 78467 Germany	Antiadiposium x-112 S Dragees
Germany	Haenseler GmbH Gottlieb - Daimler - Strasse 1 Konstanz DE 78467 Germany	Antiadiposium x-112 S Tropfen
Germany	Heinrich Mack Nachf. (Pfizer) PO Box 4949 Pfizerstraße 1 Karlsruhe DE 76139 Germany	Mirapront-N
Luxemburg	Heinrich Mack Nachf. (Pfizer) PO Box 4949 Pfizerstraße 1 Karlsruhe DE 76139 Germany	Mirapront-N

Substance: Norpseudoephedrine

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Germany	Heumann Pharma GmbH Heideloffstrasse 18-28 Nuernberg DE 90478 Germany	Amorphan Depot
Germany	Rathaus-Apotheke Ahrensboeker Strasse 28 Stockelsdorf DE 23617 Germany	Bea - Kapseln Rot-weiss
Germany	Resana Dr. Hannes Lang KG Frintroper Strasse 235 Essen DE 45359 Germany	Antiadiposium
Germany	Resana Dr. Hannes Lang KG Frintroper Strasse 235 Essen DE 45359 Germany	Schlank - Dragees Resana
Germany	Salutas Fahlberg-List Pharma GmbH Alt Salbke 60-63 Magdeburg DE 39049 Germany	Exponcit N
Germany	Schuck GmbH Industriestrasse 11 Schwaig DE 90571 Germany	Vita - Schlanktropfen Schuck

Substance: Phentermine

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
United Kingdom	3M Health Care 1 Morley Street Loughborough Leicestershire LE11 1EP United Kingdom	Duromine
Ireland	3M Health Care 1 Morley Street Loughborough Leicestershire LE11 1EP United Kingdom	Duromine
Luxembourg	Bio-Therabel SA 1001, Chaussée d'Alseberg Bruxelles BE 1180 Belgium	Panbesy Nyscaps
Belgium	Bio-Therabel SA 1001, Chaussée d'Alseberg Bruxelles BE 1180 Belgium	Panbesy Nyscaps
Portugal	Ferraz Lyace Lda Rua Rosa Aranjó 27-31 Lisboa PT 1203 Portugal	Mirapront
Ireland	Fisons Pharmaceuticals Ireland Ltd. c/o Rhone Poulenc Rorer 14 Deans Grance Industrial Estate Black Rock County Dublin Ireland	Ionamin

Substance: Phentermine

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Austria	Gerot Pharmazeutika GmbH Arnethgasse 3 Wien AT 1160 Austria	Adipex Retard
Germany	Julius Lachmann Avion Pharma GmbH & Co. Hellkamp 74 Hamburg DE 20255 Germany	Aviposan
Austria	Pfizer Corporation Austria Mondscheingasse 16 Wien AT 1070 Austria	Mirapront

Substance: Phentermine resinate

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Luxembourg	Certa S.A. Avenue de l'Artisanat, 2B Braine-L'Alleud 1420 Belgium	Ionamin-15
Belgium	Certa SA Avenue de l'Artisanat, 2B Braine L'Alleud BE 1420 Belgium	Ionamin
Luxembourg	Certa SA Avenue de l'Artisanat, 2B Braine L'Alleud BE 1420 Belgium	Ionamin Forte
Belgium	Certa SA Avenue de l'Artisanat, 2B Braine L'Alleud BE 1420 Belgium	Ionamin Forte
United Kingdom	Torbet Laboratories Limited Boughton Lane Maidstone Kent ME15 9QQ United Kingdom	Ionamin

Substance: Fenproporex

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Spain	Berenguer Infale SA (Grupo Prodes) c/ Trabajo s/n. San Just Desvern Barcelona ES 08960 Spain	Grasmin
Germany	Chephasaar Chemisch-Pharmazeut. Fabrik GmbH Muehlstrasse 50 St. Ingbert DE 66386 Germany	Fenproporex
France	Laboratoires Deglaude BP 140-58, Avenue Aristide Briand Bagneux Cedex FR 92223 France	Fenproporex action prolongée deglaude
Portugal	Laboratoires Zimaia Lda Rua de Andaluz, n. 38 Lisboa PT 1000 Portugal	Pesex-R

Substance: Fenproporex

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Spain	Laboratorios Lasa (Beaufour) Crt. Laurea Miró, 395 Sant Feliu de Llobregat Barcelona ES 08980 Spain	Dicel
Spain	Laboratorios Natterman SA Crt. Alcorcón-Leganés Km 1,8 Alcorcon Madrid ES 28925 Spain	Falagan
Portugal	Laquifa Laboratories S.A. Rua Joào de Deus, 11, Venda Nova Amadora Codex PT 2701 Portugal	Drenur
Spain	Roussel Iberica SA Avda. Castilla, 2. Parque Empresarial San Fernando de Henares Madrid ES 28831 Spain	Tegisec
Portugal	Roussel Portugal Lda Rua Joào de Deus, 19-Venda Nova Amadora Codex PT 2701 Portugal	Tegisec
Spain	Zyma Farmaceutica SA c/ Suiza, 9-11 Barcelona ES 08023 Spain	Antiobes Retard

Substance: Mazindol

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Portugal	Produtos Sandoz Lda Rua de S. Caetano 4 Lisboa PT 1119	Teronac
Greece	Sandoz 12 km, National Road Nr 1 Metamorfoisis GR 144 51 Greece	Teronac
The Netherlands	Sandoz BV Loopkantstraat 25 Uden NL 5405 AC Netherlands	Teronac
United Kingdom	Sandoz Pharmaceuticals Frimley Business Park Frimley Camberley Surrey GU16 15SG United Kingdom	Teronac

Substance: Amfepramone

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Denmark	Abigo Medical AB Datavägen 23 Askim SE 436 32 Sweden	Dobesin
Luxembourg	Asta Medica SA 77-81, rue de l'Etuve Bruxelles BE 1000 Belgium	Prefamone
Belgium	Asta Medica SA 77-81, rue de l'Etuve Bruxelles BE 1000 Belgium	Prefamone
Belgium	Asta Medica SA 77-81, rue de l'Etuve Bruxelles BE 1000 Belgium	Prefamone chronules
France	Dexo SA 31, rue d'Arras Nanterre FR 92000 France	Prefamone chronules à libération prolongée
Greece	Diapit AG. Konstantinou 6 Athens GR 10431 Greece	Linea
Italy	Gruppo Lepetit SpA Via R. Lepetit 8 Lainate (Milano) IT Italy	Tenuate Dospan

Substance: Amfepramone

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
France	Laboratoires Crinex B.P. 337, 3 Rue de Gentilly Montrouge Cedex FR 92541 France	Anorex
Belgium	Laboratoires Pharmaceutiques Trenker SA 480-482, avenue Dolez Bruxelles BE 1180 Belgium	Diethylpropion Hydrochloride
Belgium	Laboratoires Pharmaceutiques Trenker SA 480-482, avenue Dolez Bruxelles BE 1180 Belgium	Dietil - Retard
Belgium	Laboratoires Pharmaceutiques Trenker SA 480-482, avenue Dolez Bruxelles BE 1180 Belgium	Regenon
Luxembourg	Laboratoires Pharmaceutiques Trenker SA 480-482, avenue Dolez Bruxelles BE 1180 Belgium	Regenon
Luxembourg	Laboratoires Pharmaceutiques Trenker SA 480-482, avenue Dolez Bruxelles BE 1180 Belgium	Atractil

Substance: Amfepramone

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
France	Laboratoires Deglaude BP 140-58, avenue Aristide Briand Bagneux Cedex FR 92223 France	Moderatan
Belgium	Hoechst Marion Roussel SA Rue Colonel Bourg, 155 1110 Bruxelles Belgium	Menutil
Luxembourg	Hoechst Marion Roussel SA Rue Colonel Bourg, 155 1110 Bruxelles Belgium	Menutil
Belgium	Marion Merrel Dow 4, Minervastraat Zaventem BE 1930 Belgium	Tenuate Dospan
Luxembourg	Marion Merrel Dow 4, Minervastraat Zaventem BE 1930 Belgium	Tenuate Dospan
Germany	Marion Merrel Dow GmbH Komturstasse 58-62 Berlin DE 12099 Germany	Tenuate Retard
Ireland	Marion Merrel Dow Ltd. Lakeside House Stockley Park Uxbridge Middlesex UB11 1BE United Kingdom	Tenuate Dospan

Substance: Amfepramone

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
United Kingdom	Marion Merrel Dow Ltd. Lakeside House Stockley Park Uxbridge Middlesex UB11 1BE United Kingdom	Tenuate Dospan
Spain	Marion Merrel Dow SA Ctra. Madrid-Barcelona Km 25,8 Alcala de Henares Madrid ES 28800 Spain	Delgamer
France	Marion Merrel Dow SA BP74-130, rue Victor Hugo Levallois-Perret Cedex FR 92303 France	Tenuate Dospan
United Kingdom	Norton HN & Co. Ltd. Gemini House Flex Meadow Harlow Essex CM19 5TJ United Kingdom	Amfepramone
Austria	Salus-Braumapharm GmbH Industriegasse 7 Wien AT 1230 Austria	Regenon

Substance: Amfepramone

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Austria	Salus-Braumapharm GmbH Industriegasse 7 Wien AT 1230 Austria	Regenon Retard
Germany	Temmler Pharma GmbH (Asta Medica) Temmlerstrasse 2 Marburg DE 35039 Germany	Regenon
Germany	Temmler Pharma GmbH (Asta Medica) Temmlerstrasse 2 Marburg DE 35039 Germany	Regenon Retard
Denmark	Temmler Pharma GmbH (Asta Medica) Temmlerstrasse 2 Marburg DE 35039 Germany	Regenon Retard
Denmark	Temmler Pharma GmbH (Asta Medica) Temmlerstrasse 2 Marburg DE 35039 Germany	Regenon

Substance: Amfepramone

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Italy	Valeas SpA Via Vallisneri 10 Milano IT Italy	Linea Valeas
United Kingdom	Wyeth & Brother Ltd Huntercombe Lane South Taplow Maidenhead Berkshire SL6 OPH United Kingdom	Apisate
Ireland	Wyeth & Brother Ltd Huntercombe Lane South Taplow Maidenhead Berkshire SL6 OPH United Kingdom	Apisate

Substance: Amfepramone resinate

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Belgium	Laboratoires Pharmaceutiques Trenker SA 480-482, avenue Dolez Bruxelles BE 1180 Belgium	Atractil
Belgium	Laboratoires Pharmaceutiques Trenker SA 480-482, avenue Dolez Bruxelles BE 1180 Belgium	Diethylpropion Poudre

Substance: Phendimetrazine

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Belgium	Labima S.A. Avenue d'Uccle 34 Bruxelles BE 1190 Belgium	Anoran
Italy	Wyeth SpA Via Nettunense 90 Aprilia (Latina) IT 04011 Italy	Plegine

Substance: Phenmetrazine

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Germany	Ravensberg GmbH Chemische Fabrik Schneckenburgstrasse 46 Konstanz DE 78467 Germany	Cafilon

Substance: Mefenorex

Member State	Marketing Authorisation Holder	Name of the Medicinal Product
Germany	Asta Medica AG Weismüllerstrasse 44-45 Frankfurt DE 60314 Germany	Rondimen
France	Pierre Fabre Santé 45, Place Abel Gance Boulogne Cedex FR 92654 France	Incital

ANNEX II

AMENDMENTS TO THE TERMS OF THE NATIONAL MARKETING AUTHORISATIONS OF MEDICINAL PRODUCTS TO BE INTRODUCED

**Excerpt of the Summary Product Characteristics (as defined in article 4a of Council
Directive 65/65/EEC as amended) :**

CLINICAL PARTICULARS

Therapeutic indications

Adjunctive therapy to diet, in patients with obesity and a body mass index (BMI) of 30 kg/m² or higher who have not responded to an appropriate weight-reducing regimen alone.

Note: short-term efficacy only has been demonstrated with regard to weight reduction. No significant data on changes in morbidity or mortality are yet available.

Posology and method of administration

It is recommended that treatment should be conducted under the care of physicians experienced in the treatment of obesity.

Secondary organic causes of obesity must be excluded by diagnosis before prescribing this agent.

The management of obesity should be undertaken using a global approach which should include dietary, medical and psychotherapeutic methods.

Evening dosing should be avoided, as this agent may induce nervousness and insomnia

Duration of treatment

The duration of treatment is 4-6 weeks and should not exceed three months.

Contraindications

- Pulmonary artery hypertension
- Severe arterial hypertension
- Current or past medical history of cardio-vascular or cerebro-vascular disease
- Current or past medical history of psychiatric disorders including anorexia nervosa and depression,
- Propensity towards drug abuse, known alcoholism.
- Children below 12 years.

Combination drug therapy with any other centrally acting anorectic agent is contraindicated due to the increased risk of potentially fatal pulmonary artery hypertension.

Special warnings and precautions for use

Special warnings

Cases of severe, often fatal, pulmonary artery hypertension, have been reported in patients who have received anorectics of the type in this product. An epidemiological study has shown that anorectic intake is a risk factor involved in the development of pulmonary artery hypertension and that the use of anorectics is strongly associated with an increased risk for this adverse drug reaction. In view of this rare but serious risk, it must be emphasised that :

- **careful compliance with the indication and the duration of treatment is required,**
- **duration of treatment greater than 3 months and a BMI ≥ 30 kg/m² increase the risk of pulmonary artery hypertension,**
- **the onset or aggravation of exertional dyspnea suggests the possibility of occurrence of pulmonary artery hypertension. Under these circumstances, treatment should be immediately discontinued and the patient referred to a specialist unit for investigation.**

Special precautions for use

- Prolonged treatment may give rise to pharmacological tolerance and drug dependence, and more rarely to severe psychotic disorders in predisposed patients.
- Rarely, cases of cardiac and cerebro-vascular accidents have been reported, often following rapid weight loss. Special care should be taken to ensure gradual and controlled weight loss in obese patients, who are subjects to a risk of vascular disease. This anorectic agent should not be prescribed in patients with current or a past medical history of cardio-vascular or cerebro-vascular disease.
- This anorectic agent should be used with caution in epileptic patients

Undesirable effects

- An epidemiological study has shown that anorectic intake is a risk factor involved in the development of pulmonary artery hypertension and that the use of anorectics is strongly associated with an increased risk for this adverse drug reaction. Cases of pulmonary artery hypertension have been reported in patients treated with this agent. Pulmonary artery hypertension is a severe and often fatal disease. The occurrence or aggravation of exertional dyspnea is usually the first clinical sign and requires treatment discontinuation and investigation in a specialised unit (see special warnings).

CNS effects :

- the prolonged use of this agent is associated with a risk of pharmacological tolerance, dependence and withdrawal syndrome
- the most common adverse reactions which have been described are : psychotic reactions or psychosis, depression, nervousness, agitation, sleep disorders and vertigo
- convulsions have been reported

Cardio-vascular effects:

- the most common reported reactions are tachycardia, palpitations, hypertension, precordial pain
- rarely cases of cardiovascular or cerebro-vascular accidents have been described in patients treated with anorectic agents. In particular stroke, angina, myocardial infarction, cardiac failure and cardiac arrest have been reported.