ANNEX I

LIST OF THE NAMES, PHARMACEUTICAL FORM, STRENGTH OF THE MEDICINAL PRODUCT, ROUTES OF ADMINISTRATION, MARKETING AUTHORISATION HOLDERS IN THE MEMBER STATES

Member State	**Marketing Authorisation Holder**	**Invented Name**	**Strength**	**Pharmaceutical Form**	**Route of Administration**
Austria	AstraZeneca Őesterreich GmbH Schwarzenbergplatz 7 A -1037 Wien	Arimidex	1 mg	Film-coated Tablets	Oral
Belgium	NV AstraZeneca SA Egide Van Ophemstraat B-1180 Brussel	Arimidex	1 mg	Film-coated Tablets	Oral
Bulgaria	AstraZeneca Pharmaceuticals AB S-15185 Södertälje Sweden	Arimidex	1 mg	Film-coated Tablets	Oral
Cyprus	AstraZeneca UK LTD Silk Road Business Park Macclesfield Cheshire SK10 2NA UK	Arimidex	1 mg	Film-coated Tablets	Oral
Czech Republic	AstraZeneca UK Ltd Silk Road Business Park Macclesfield Cheshire SK10 2NA Velká Británie	Arimidex	1 mg	Film-coated Tablets	Oral
Denmark	AstraZeneca A/S Roskildevej 22 2620 Albertslund	Arimidex	1 mg	Film-coated Tablets	Oral
Estonia	AstraZeneca UK Ltd Stanhope Gate 15 London W1K 1LN Ühendkuningriik	Arimidex	1 mg	Film-coated Tablets	Oral
Finland	AstraZeneca Oy Luomanportti 3 FI-02200 Espoo, Finland	Arimidex	1 mg	Film-coated Tablets	Oral
France	AstraZeneca 1 place Renault 92844 Rueil-Malmaison Cedex	Arimidex	1 mg	Film-coated Tablets	Oral

Member State	Marketing Authorisation Holder	Invented Name	Strength	Pharmaceutical Form	Route of Administration
Germany	AstraZeneca GmbH 22876 Wedel	Arimidex	1 mg	Film-coated Tablets	Oral
Greece	AstraZeneca S.A. 4 Theotokopoulou & Astronafton str 151 25 Maroussi Athens, Greece	Arimidex	1 mg	Film-coated Tablets	Oral
Hungary	AstraZeneca Kft. 2045 Törökbálint Park u 3. Magyarország	Arimidex	1 mg	Film-coated Tablets	Oral
Iceland	AstraZeneca UK Ltd Silk Road Business Park Macclesfield Cheshire, United Kingdom	Arimidex	1 mg	Film-coated Tablets	Oral
Ireland	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, UK.	Arimidex	1 mg	Film-coated Tablets	Oral
Italy	AstraZeneca S.p.A. Palazzo Volta - Via F. Sforza 20080 - Basiglio (Milano) Italia	Arimidex	1 mg	Film-coated Tablets	Oral
Latvia	AstraZeneca UK Limited, Silk Road Business Park Macclesfield, Cheshire, SK 10 2 NA, UK	Arimidex	1 mg	Film-coated Tablets	Oral
Lithuania	AstraZeneca UK Limited Silk Road Business Park Macclesfield Cheshire SK 10 2NA United Kingdom	Arimidex	1 mg	Film-coated Tablets	Oral

Member State	**Marketing Authorisation Holder**	**Invented Name**	**Strength**	**Pharmaceutical Form**	**Route of Administration**
Luxembourg	NV AstraZeneca SA Rue Egide Van Ophem B-1180 Bruxelles	Arimidex	1 mg	Film-coated Tablets	Oral
Malta	AstraZeneca UK Limited Silk Road Business Park Macclesfield Cheshire SK10 2NA United Kingdom	Arimidex	1 mg	Film-coated Tablets	Oral
Netherlands	AstraZeneca BV Louis Pasteurlaan 5 2719 EE Zoetermeer	Arimidex	1 mg	Film-coated Tablets	Oral
Norway	AstraZeneca AS Hoffsveien 70B, Box 200 Vinderen 0319 Oslo, Norway	Arimidex	1 mg	Film-coated Tablets	Oral
Poland	AstraZeneca UK Limited Silk Road Business Park Macclesfield Cheshire SK10 2NA Wielka Brytania	Arimidex	1 mg	Film-coated Tablets	Oral
Portugal	AstraZeneca Produtos Farmacêuticos, Lda. Rua Humberto Madeira, 7 Valejas 2745-663 Barcarena	Arimidex	1 mg	Film-coated Tablets	Oral
Romania	AstraZeneca UK Limited 600 Capability Green Luton LU1 3LU UK	Arimidex	1 mg	Film-coated Tablets	Oral

Member State	**Marketing Authorisation Holder**	**Invented Name**	**Strength**	**Pharmaceutical Form**	**Route of Administration**
Slovakia	AstraZeneca UK Limited Silk Road Business Park Macclesfield Cheshire SK 10 2NA United Kingdom	Arimidex	1 mg	Film-coated Tablets	Oral
Slovenia	AstraZeneca UK Limited, 15 Stanhope Gate, London W1K 1LN Velika Britanija	Arimidex 1 mg film coated tablets	1 mg	Film-coated Tablets	Oral
Spain	AstraZeneca Farmacéutica Spain, S.A. Parque Norte Edificio Roble C/ Serrano Galvache 56 – 28033 Madrid	Arimidex	1 mg	Film-coated Tablets	Oral
Sweden	AstraZeneca AB 151 85 Södertälje	Arimidex	1 mg	Film-coated Tablets	Oral
United Kingdom	AstraZeneca UK Limited 600 Capability Green Luton LU1 3LU, UK	Arimidex	1 mg	Film-coated Tablets	Oral

ANNEX II

AMENDMENT TO SUMMARY OF PRODUCT CHARACTERISTICS

AMENDMENTS TO BE INCLUDED IN THE RELEVANT SECTIONS OF THE SUMMARY OF PRODUCT CHARACTERISTICS FOR ARIMIDEX.

4.2 Posology and method of administration

[……]
Children

Arimidex is not recommended for use in children due to insufficient data on safety and efficacy (see sections 4.4 and 5.1).
[……]

4.4 Special warnings and precautions for use

[……]
Arimidex is not recommended for use in children as safety and efficacy have not been established in this group of patients (see section 5.1).

Arimidex should not be used in boys with growth hormone deficiency in addition to growth hormone treatment. In the pivotal clinical trial, efficacy was not demonstrated and safety was not established (see section 5.1). Since anastrozole reduces oestradiol levels, Arimidex must not be used in girls with growth hormone deficiency in addition to growth hormone treatment. Long-term safety data in children and adolescents are not available.
[……]

5.1 Pharmacodynamic properties

[……]
Paediatrics

Arimidex is not indicated for use in children. Efficacy has not been established in the paediatric populations studied (see below). The number of children treated was too limited to draw any reliable conclusions on safety. No data on the potential long-term effects of anastrozole treatment in children are available (see also section 5.3).

The European Medicines Agency has waived the obligation to submit the results of studies with Arimidex in one or several subsets of the paediatric population in short stature due to growth hormone deficiency (GHD), testotoxicosis, gynaecomastia, and McCune-Albright syndrome.

Short stature due to growth hormone deficiency
A randomised, double-blind, multi-centre study evaluated 52 pubertal boys (aged 11-16 years inclusive) with GHD treated for 12 to 36 months with Arimidex 1 mg/day or placebo in combination with growth hormone. Only 14 subjects on anastrozole completed 36 months.

After 3 years anastrozole was found to statistically significantly slow bone maturation in pubertal boys on growth hormone therapy. No statistically significant difference with placebo was observed for the growth related parameters of predicted adult height, height, height SDS, and height velocity. Final height data were not available. While the number of children treated was too limited to draw any reliable conclusions on safety, there was an increased fracture rate and a trend towards reduced bone mineral density in the anastrozole arm compared to placebo.

Testotoxicosis

An open-label, non-comparative, multi-centre study evaluated 14 male patients (aged 2-9) with familial male-limited precocious puberty, also known as testotoxicosis, treated with combination of Arimidex and bicalutamide. The primary objective was to assess the efficacy and safety of this combination regimen over 12 months. Thirteen out of the 14 patients enrolled completed 12 months of combination treatment (one patient was lost to follow-up). There was no significant difference in growth rate after 12 months of treatment, relative to the growth rate during the 6 months prior to entering the study.

5.3 Preclinical safety data

[……]

In a fertility study weanling male rats were dosed orally with 50 or 400 mg/l anastrozole via their drinking water for 10 weeks. Measured mean plasma concentrations were 44.4 (± 14.7) ng/ml and 165 (±90) ng/ml respectively. Mating indices were adversely affected in both dose groups, whilst a reduction in fertility was evident only at the 400 mg/l dose level. The reduction was transient as all mating and fertility parameters were similar to control group values following a 9-week treatment-free recovery period.

ANNEX III

CONDITIONS OF THE MARKETING AUTHORISATION

The National Health Authorities, coordinated by the Reference Member State, shall ensure the following conditions are fulfilled by the Marketing Authorisation Holder:

The Applicant commits to the following:

- Submit a Risk Management Plan (or its update) for Arimidex at National level, taking into account the new paediatric data and the CHMP recommendations.
- Ensure that the Package Leaflet in all languages contains a statement referring to the fact that Arimidex should not be given to children.