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 EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Austria	AstraZeneca Österreich GmbH., Schwarzenbergplatz 7, A-1037 Wien, Austria	Atacand 2 mg - Tabletten	2 mg	Tablet	Oral use
Austria	AstraZeneca Österreich GmbH., Schwarzenbergplatz 7, A-1037 Wien, Austria	Atacand 4 mg - Tabletten	4 mg	Tablet	Oral use
Austria	AstraZeneca Österreich GmbH., Schwarzenbergplatz 7, A-1037 Wien, Austria	Atacand 8 mg - Tabletten	8 mg	Tablet	Oral use
Austria	AstraZeneca Österreich GmbH., Schwarzenbergplatz 7, A-1037 Wien, Austria	Atacand 16 mg - Tabletten	16 mg	Tablet	Oral use
Austria	AstraZeneca Österreich GmbH., Schwarzenbergplatz 7, A-1037 Wien, Austria	Atacand 32 mg - Tabletten	32 mg	Tablet	Oral use
Austria	Takeda Pharma Ges.m.b.H. Seidengasse 33-35 1070 Wien Austria	Blopress 4 mg – Tabletten	4 mg	Tablet	Oral use
Austria	Takeda Pharma Ges.m.b.H. Seidengasse 33-35 1070 Wien Austria	Blopress 8 mg – Tabletten	8 mg	Tablet	Oral use
Austria	Takeda Pharma Ges.m.b.H. Seidengasse 33-35 1070 Wien Austria	Blopress 16 mg – Tabletten	16 mg	Tablet	Oral use
Austria	Takeda Pharma Ges.m.b.H. Seidengasse 33-35 1070 Wien Austria	Blopress 32 mg – Tabletten	32 mg	Tablet	Oral use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Belgium	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	2 mg	Tablet	Oral use
Belgium	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	4 mg	Tablet	Oral use
Belgium	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	8 mg	Tablet	Oral use
Belgium	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	16 mg	Tablet	Oral use
Belgium	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	32 mg	Tablet	Oral use
Bulgaria	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand	8 mg	Tablet	Oral use
Bulgaria	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand	16 mg	Tablet	Oral use
Bulgaria	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand	32 mg	Tablet	Oral use
Cyprus	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand	4 mg	Tablet	Oral use
Cyprus	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand	8 mg	Tablet	Oral use
Cyprus	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand	16 mg	Tablet	Oral use
Cyprus	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand	32 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Czech Republic	AstraZeneca UK Ltd., Macclesfield, Cheshire, United Kingdom	Atacand 4 mg	4 mg	Tablet	Oral use
Czech Republic	AstraZeneca UK Ltd., Macclesfield, Cheshire, United Kingdom	Atacand 8 mg	8 mg	Tablet	Oral use
Czech Republic	AstraZeneca UK Ltd., Macclesfield, Cheshire, United Kingdom	Atacand 16 mg	16 mg	Tablet	Oral use
Denmark	AstraZeneca A/S Roskildevej 22 DK-2620 Albertslund, Denmark	Atacand	4 mg	Tablet	Oral use
Denmark	AstraZeneca A/S Roskildevej 22 DK-2620 Albertslund, Denmark	Atacand	8 mg	Tablet	Oral use
Denmark	AstraZeneca A/S Roskildevej 22 DK-2620 Albertslund, Denmark	Atacand	16 mg	Tablet	Oral use
Denmark	AstraZeneca A/S Roskildevej 22 DK-2620 Albertslund, Denmark	Atacand	32 mg	Tablet	Oral use
Estonia	AstraZeneca AB, Strängnäsvägen 44, S-151 85 Södertälje, Sweden	Atacand	8 mg	Tablet	Oral use
Estonia	AstraZeneca AB, Strängnäsvägen 44, S-151 85 Södertälje, Sweden	Atacand	16 mg	Tablet	Oral use
Estonia	AstraZeneca AB, Strängnäsvägen 44, S-151 85 Södertälje, Sweden	Atacand	32 mg	Tablet	Oral use
Finland	AstraZeneca Oy Luomanportti 3 FI-02200 Espoo Finland	Atacand	2 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Finland	AstraZeneca Oy Luomanportti 3 FI-02200 Espoo Finland	Atacand	4 mg	Tablet	Oral use
Finland	AstraZeneca Oy Luomanportti 3 FI-02200 Espoo Finland	Atacand	8 mg	Tablet	Oral use
Finland	AstraZeneca Oy Luomanportti 3 FI-02200 Espoo Finland	Atacand	16 mg	Tablet	Oral use
Finland	AstraZeneca Oy Luomanportti 3 FI-02200 Espoo Finland	Atacand	32 mg	Tablet	Oral use
France	AstraZeneca 1, Place Renault 92844 Rueil- Malmaison Cedex France	Atacand 4 mg, comprimé sécable	4 mg	Tablet	Oral use
France	AstraZeneca 1, Place Renault 92844 Rueil- Malmaison Cedex France	Atacand 8 mg, comprimé sécable	8 mg	Tablet	Oral use
France	AstraZeneca 1, Place Renault 92844 Rueil- Malmaison Cedex France	Atacand 16 mg, comprimé sécable	16 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
France	AstraZeneca 1, Place Renault 92844 Rueil- Malmaison Cedex France	Atacand 32 mg, comprimé sécable	32 mg	Tablet	Oral use
France	Laboratoires Takeda 11-15, quai de Dion Bouton 92816 Puteaux Cedex France	Kenzen 4 mg, comprimé sécable	4 mg	Tablet	Oral use
France	Laboratoires Takeda 11-15, quai de Dion Bouton 92816 Puteaux Cedex France	Kenzen 8 mg, comprimé sécable	8 mg	Tablet	Oral use
France	Laboratoires Takeda 11-15, quai de Dion Bouton 92816 Puteaux Cedex France	Kenzen 16 mg, comprimé sécable	16 mg	Tablet	Oral use
France	Laboratoires Takeda 11-15, quai de Dion Bouton 92816 Puteaux Cedex France	Kenzen 32 mg, comprimé sécable	32 mg	Tablet	Oral use
Germany	AstraZeneca GmbH 22876 Wedel, Germany	Atacand 4 mg	4 mg	Tablet	Oral use
Germany	AstraZeneca GmbH 22876 Wedel, Germany	Atacand 8 mg	8mg	Tablet	Oral use
Germany	AstraZeneca GmbH 22876 Wedel, Germany	Atacand 16 mg	16 mg	Tablet	Oral use
Germany	AstraZeneca GmbH 22876 Wedel, Germany	Atacand PROTECT 32 mg Tabletten	32mg	Tablet	Oral use
Germany	Takeda Pharma GmbH Viktoriaallee 3-5 52066 Aachen Germany	Blopress 2 mg Tabletten	2 mg	Tablet	Oral use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Germany	Takeda Pharma GmbH Viktoriaallee 3-5 52066 Aachen Germany	Blopress 4 mg Tabletten	4 mg	Tablet	Oral use
Germany	Takeda Pharma GmbH Viktoriaallee 3-5 52066 Aachen Germany	Blopress 8 mg Tabletten	8 mg	Tablet	Oral use
Germany	Takeda Pharma GmbH Viktoriaallee 3-5 52066 Aachen Germany	Blopress 16 mg Tabletten	16 mg	Tablet	Oral use
Germany	Takeda Pharma GmbH Viktoriaallee 3-5 52066 Aachen Germany	Blopress 32 mg Tabletten	32 mg	Tablet	Oral use
Greece	AstraZeneca SA Theotokopoulou 4 & Astrnafton 151 25 Maroussi Greece	Atacand	2 mg	Tablet	Oral use
Greece	AstraZeneca SA Theotokopoulou 4 & Astronafton 151 25 Maroussi Greece	Atacand	4 mg	Tablet	Oral use
Greece	AstraZeneca SA Theotokopoulou 4 & Astronafton 151 25 Maroussi Greece	Atacand	8 mg	Tablet	Oral use
Greece	AstraZeneca SA Theotokopoulou 4 & Astronafton 151 25 Maroussi Greece	Atacand	16 mg	Tablet	Oral use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Greece	AstraZeneca SA Theotokopoulou 4 & Astronafton 151 25 Maroussi Greece	Atacand	32 mg	Tablet	Oral use
Hungary	AstraZeneca Kft. 1113 Budapest, Bocskai út 134-146 Hungary	Atacand	8 mg	Tablet	Oral use
Hungary	AstraZeneca Kft. 1113 Budapest, Bocskai út 134-146 Hungary	Atacand	16 mg	Tablet	Oral use
Iceland	AstraZeneca A/S Roskildevej 22, DK-2620 Albertslund, Denmark	Atacand	4 mg	Tablet	Oral use
Iceland	AstraZeneca A/S Roskildevej 22, DK-2620 Albertslund, Denmark	Atacand	8 mg	Tablet	Oral use
Iceland	AstraZeneca A/S Roskildevej 22, DK-2620 Albertslund, Denmark	Atacand	16 mg	Tablet	Oral use
Iceland	AstraZeneca A/S Roskildevej 22, DK-2620 Albertslund, Denmark	Atacand	32 mg	Tablet	Oral use
Ireland	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	2 mg	Tablet	Oral use
Ireland	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	4 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Ireland	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	8 mg	Tablet	Oral use
Ireland	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	16 mg	Tablet	Oral use
Ireland	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	32 mg	Tablet	Oral use
Ireland	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Blopress 2 mg	2 mg	Tablet	Oral use
Ireland	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Blopress 4 mg	4 mg	Tablet	Oral use
Ireland	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Blopress 8 mg	8 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Ireland	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Blopress 16 mg	16 mg	Tablet	Oral use
Ireland	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Blopress 32 mg	32 mg	Tablet	Oral use
Italy	AstraZeneca SpA Palazzo Volta, via F.Sforza – 20080 Basiglio (MI) -Italy	Ratacand	2 mg	Tablet	Oral use
Italy	AstraZeneca SpA Palazzo Volta, via F.Sforza – 20080 Basiglio (MI) -Italy	Ratacand	4 mg	Tablet	Oral use
Italy	AstraZeneca SpA Palazzo Volta, via F.Sforza – 20080 Basiglio (MI) -Italy	Ratacand	8mg	Tablet	Oral use
Italy	AstraZeneca SpA Palazzo Volta, via F.Sforza – 20080 Basiglio (MI) -Italy	Ratacand	16 mg	Tablet	Oral use
Italy	AstraZeneca SpA Palazzo Volta, via F.Sforza – 20080 Basiglio (MI) -Italy	Ratacand	32 mg	Tablet	Oral use
Italy	Takeda Italia Farmaceutici S.p.A. Via Elio Vittorini, 129 00144 Roma Italy	Blopress 2 mg	2 mg	Tablet	Oral use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Italy	Takeda Italia Farmaceutici S.p.A. Via Elio Vittorini, 129 00144 Roma Italy	Blopress 4 mg	4 mg	Tablet	Oral use
Italy	Takeda Italia Farmaceutici S.p.A. Via Elio Vittorini, 129 00144 Roma Italy	Blopress 8 mg	8 mg	Tablet	Oral use
Italy	Takeda Italia Farmaceutici S.p.A. Via Elio Vittorini, 129 00144 Roma Italy	Blopress 16 mg	16 mg	Tablet	Oral use
Italy	Takeda Italia Farmaceutici S.p.A. Via Elio Vittorini, 129 00144 Roma Italy	Blopress 32 mg	32 mg	Tablet	Oral use
Latvia	AstraZeneca AB S-151 85 Södertälje, Sweden	Atacand	8 mg	Tablet	Oral use
Latvia	AstraZeneca AB S-151 85 Södertälje, Sweden	Atacand	16 mg	Tablet	Oral use
Lithuania	AstraZeneca AB S-151 85 Södertälje, Sweden	Atacand	4 mg	Tablet	Oral use
Lithuania	AstraZeneca AB S-151 85 Södertälje, Sweden	Atacand	8 mg	Tablet	Oral use
Lithuania	AstraZeneca AB S-151 85 Södertälje, Sweden	Atacand	16 mg	Tablet	Oral use
Lithuania	AstraZeneca AB S-151 85 Södertälje, Sweden	Atacand	32 mg	Tablet	Oral use
Luxembourg	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	2 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Luxembourg	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	4 mg	Tablet	Oral use
Luxembourg	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	8mg	Tablet	Oral use
Luxembourg	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	16 mg	Tablet	Oral use
Luxembourg	NV AstraZeneca SA Egide Van Ophemstraat 110 B-1180 Brussels Belgium	Atacand	32 mg	Tablet	Oral use
Malta	AstraZeneca AB, Gärtunavägen, S-15185, Södertälje, Sweden	Atacand	8 mg	Tablet	Oral use
Malta	AstraZeneca AB, Gärtunavägen, S-15185, Södertälje, Sweden	Atacand	16 mg	Tablet	Oral use
Netherlands	AstraZeneca BV Louis Pasteurlaan 5 2719 EE Zoetermeer The Netherlands	Atacand 2, tabletten 2 mg	2 mg	Tablet	Oral use
Netherlands	AstraZeneca BV Louis Pasteurlaan 5 2719 EE Zoetermeer The Netherlands	Atacand 4, tabletten 4 mg	4 mg	Tablet	Oral use
Netherlands	AstraZeneca BV Louis Pasteurlaan 5 2719 EE Zoetermeer The Netherlands	Atacand 8, tabletten 8 mg	8 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Netherlands	AstraZeneca BV Louis Pasteurlaan 5 2719 EE Zoetermeer The Netherlands	Atacand 16, tabletten 16 mg	16 mg	Tablet	Oral use
Netherlands	AstraZeneca BV Louis Pasteurlaan 5 2719 EE Zoetermeer The Netherlands	Atacand 32, tabletten 32 mg	32 mg	Tablet	Oral use
Norway	AstraZeneca AS Boks 200 Vinderen NO-0319 Oslo, Norway	Atacand	4 mg	Tablet	Oral use
Norway	AstraZeneca AS Boks 200 Vinderen NO-0319 Oslo, Norway	Atacand	8mg	Tablet	Oral use
Norway	AstraZeneca AS Boks 200 Vinderen NO-0319 Oslo , Norway	Atacand	16 mg	Tablet	Oral use
Norway	AstraZeneca AS Boks 200 Vinderen NO-0319 Oslo, Norway	Atacand	32mg	Tablet	Oral use
Poland	AstraZeneca AB, S-151 85 Södertälje, Gärtunavägen, Sweden	Atacand	4 mg	Tablet	Oral use
Poland	AstraZeneca AB, S-151 85 Södertälje, Gärtunavägen, Sweden	Atacand	8 mg	Tablet	Oral use
Poland	AstraZeneca AB, S-151 85 Södertälje, Gärtunavägen, Sweden	Atacand	16 mg	Tablet	Oral use
Poland	AstraZeneca AB, S-151 85 Södertälje, Gärtunavägen, Sweden	Atacand	32 mg	Tablet	Oral use
Portugal	AstraZeneca Produtos Farmacêuticos, Lda. Rua Humberto Madeira, 7, Valejas 2745-663 Barcarena, Portugal	Atacand	2 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Portugal	AstraZeneca Produtos Farmacêuticos, Lda. Rua Humberto Madeira, 7, Valejas 2745-663 Barcarena, Portugal	Atacand	4 mg	Tablet	Oral use
Portugal	AstraZeneca Produtos Farmacêuticos, Lda. Rua Humberto Madeira, 7, Valejas 2745-663 Barcarena, Portugal	Atacand	8 mg	Tablet	Oral use
Portugal	AstraZeneca Produtos Farmacêuticos, Lda. Rua Humberto Madeira, 7, Valejas 2745-663 Barcarena, Portugal	Atacand	16 mg	Tablet	Oral use
Portugal	AstraZeneca Produtos Farmacêuticos, Lda. Rua Humberto Madeira, 7, Valejas 2745-663 Barcarena, Portugal	Atacand 32 mg	32 mg	Tablet	Oral use
Portugal	Lusomedicamenta - Sociedade Técnica Farmacêutica, S.A. Estrada Consiglieri Pedroso, 69 B - Queluz de Baixo 2730-055 Barcarena Portugal	Blopress	2 mg	Tablet	Oral use
Portugal	Lusomedicamenta - Sociedade Técnica Farmacêutica, S.A. Estrada Consiglieri Pedroso, 69 B - Queluz de Baixo 2730-055 Barcarena Portugal	Blopress	4 mg	Tablet	Oral use
Portugal	Lusomedicamenta - Sociedade Técnica Farmacêutica, S.A. Estrada Consiglieri Pedroso, 69 B - Queluz de Baixo 2730-055 Barcarena Portugal	Blopress	8 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Portugal	Lusomedicamenta - Sociedade Técnica Farmacêutica, S.A. Estrada Consiglieri Pedroso, 69 B - Queluz de Baixo 2730-055 Barcarena Portugal	Blopress	16 mg	Tablet	Oral use
Portugal	Lusomedicamenta - Sociedade Técnica Farmacêutica, S.A. Estrada Consiglieri Pedroso, 69 B - Queluz de Baixo 2730-055 Barcarena Portugal	Blopress	32 mg	Tablet	Oral use
Romania	AstraZeneca AB, S 151 85, Södertälje, Sweden	Atacand 8 mg	8 mg	Tablet	Oral use
Romania	AstraZeneca AB, S 151 85, Södertälje, Sweden	Atacand 16 mg	16 mg	Tablet	Oral use
Romania	AstraZeneca AB, S 151 85, Södertälje, Sweden	Atacand 32 mg	32 mg	Tablet	Oral use
Slovak Republic	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand 8 mg	8 mg	Tablet	Oral use
Slovak Republic	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand 16 mg	16 mg	Tablet	Oral use
Slovak Republic	AstraZeneca AB, S-151 85 Södertälje, Sweden	Atacand 32 mg	32 mg	Tablet	Oral use
Slovenia	AstraZeneca UK Limited 15 Stanhope Gate London W1K 1LN United Kingdom	Atacand 4 mg	4 mg	Tablet	Oral use
Slovenia	AstraZeneca UK Limited 15 Stanhope Gate London W1K 1LN United Kingdom	Atacand 8 mg	8 mg	Tablet	Oral use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Slovenia	AstraZeneca UK Limited 15 Stanhope Gate London W1K 1LN United Kingdom	Atacand 16 mg	16 mg	Tablet	Oral use
Slovenia	AstraZeneca UK Limited 15 Stanhope Gate London W1K 1LN United Kingdom	Atacand 32 mg	32 mg	Tablet	Oral use
Spain	AstraZeneca Farmacéutica Spain, S.A. Parque Norte.Edificio Roble. C/ Serrano Galvache 56 28033 Madrid, Spain	Atacand 4 mg comprimidos	4 mg	Tablet	Oral use
Spain	AstraZeneca Farmacéutica Spain, S.A. Parque Norte.Edificio Roble. C/ Serrano Galvache 56 28033 Madrid, Spain	Atacand 8 mg comprimidos	8mg	Tablet	Oral use
Spain	AstraZeneca Farmacéutica Spain, S.A. Parque Norte.Edificio Roble. C/ Serrano Galvache 56 28033 Madrid, Spain	Atacand 16 mg comprimidos	16 mg	Tablet	Oral use
Spain	AstraZeneca Farmacéutica Spain, S.A. Parque Norte.Edificio Roble. C/ Serrano Galvache 56 28033 Madrid, Spain	Atacand 32 mg comprimidos	32 mg	Tablet	Oral use
Spain	Takeda Global Research and Development Centre (Europe) Ltd 61 Aldwych London WC2B 4AE United Kingdom	Blopress 4 mg comprimidos	4 mg	Tablet	Oral use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Spain	Takeda Global Research and Development Centre (Europe) Ltd 61 Aldwych London WC2B 4AE United Kingdom	Blopress 8 mg comprimidos	8 mg	Tablet	Oral use
Spain	Takeda Global Research and Development Centre (Europe) Ltd 61 Aldwych London WC2B 4AE United Kingdom	Blopress 16 mg comprimidos	16 mg	Tablet	Oral use
Spain	Takeda Global Research and Development Centre (Europe) Ltd 61 Aldwych London WC2B 4AE United Kingdom	Blopress 32 mg comprimidos	32 mg	Tablet	Oral use
Spain	Almirall, S.A. Ronda General Mitre, 151 08022 Barcelona Spain	Parapres 4 mg comprimidos	4 mg	Tablet	Oral use
Spain	Almirall, S.A. Ronda General Mitre, 151 08022 Barcelona Spain	Parapres 8 mg comprimidos	8 mg	Tablet	Oral use
Spain	Almirall, S.A. Ronda General Mitre, 151 08022 Barcelona Spain	Parapres 16 mg comprimidos	16 mg	Tablet	Oral use
Spain	Almirall, S.A. Ronda General Mitre, 151 08022 Barcelona Spain	Parapres 32 mg comprimidos	32 mg	Tablet	Oral use
Sweden	AstraZeneca AB 151 85 Södertälje, Sweden	Atacand	2 mg	Tablet	Oral use
Sweden	AstraZeneca AB 151 85 Södertälje, Sweden	Atacand	4 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Sweden	AstraZeneca AB 151 85 Södertälje, Sweden	Atacand	8 mg	Tablet	Oral use
Sweden	AstraZeneca AB 151 85 Södertälje, Sweden	Atacand	16 mg	Tablet	Oral use
Sweden	AstraZeneca AB 151 85 Södertälje, Sweden	Atacand	32 mg	Tablet	Oral use
Sweden	AstraZeneca AB 151 85 Södertälje, Sweden	Racanda	4 mg	Tablet	Oral use
Sweden	AstraZeneca AB 151 85 Södertälje, Sweden	Racanda	8mg	Tablet	Oral use
Sweden	AstraZeneca AB 151 85 Södertälje, Sweden	Racanda	16 mg	Tablet	Oral use
Sweden	AstraZeneca AB 151 85 Södertälje, Sweden	Racanda	32 mg	Tablet	Oral use
United Kingdom	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	2 mg	Tablet	Oral use
United Kingdom	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	4 mg	Tablet	Oral use
United Kingdom	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	8 mg	Tablet	Oral use
United Kingdom	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	16 mg	Tablet	Oral use
United Kingdom	AstraZeneca UK Limited, 600 Capability Green, Luton, LU1 3LU, United Kingdom	Atacand	32 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
United Kingdom	Takeda Global Research and Development Centre (Europe) Ltd 61 Aldwych London WC2B 4AE United Kingdom	Blopress 2 mg	2 mg	Tablet	Oral use
United Kingdom	Takeda Global Research and Development Centre (Europe) Ltd 61 Aldwych London WC2B 4AE United Kingdom	Blopress 4 mg	4 mg	Tablet	Oral use
United Kingdom	Takeda Global Research and Development Centre (Europe) Ltd 61 Aldwych London WC2B 4AE United Kingdom	Blopress 8 mg	8 mg	Tablet	Oral use
United Kingdom	Takeda Global Research and Development Centre (Europe) Ltd 61 Aldwych London WC2B 4AE United Kingdom	Blopress 16 mg	16 mg	Tablet	Oral use
United Kingdom	Takeda Global Research and Development Centre (Europe) Ltd 61 Aldwych London WC2B 4AE United Kingdom	Blopress 32 mg	32 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
United Kingdom	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Amias 2 mg	2 mg	Tablet	Oral use
United Kingdom	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Amias 4 mg	4 mg	Tablet	Oral use
United Kingdom	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Amias 8 mg	8 mg	Tablet	Oral use
United Kingdom	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Amias 16 mg	16 mg	Tablet	Oral use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
United Kingdom	Takeda UK Limited Takeda House, Mercury Park, Wycombe Lane, Wooburn Green, High Wycombe, Buckinghamshire HP10 OHH United Kingdom	Amias 32 mg	32 mg	Tablet	Oral use

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET PRESENTED BY THE EUROPEAN MEDICINE AGENCY

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF ATACAND AND ASSOCIATED NAMES (SEE ANNEX I)

Atacand contains candesartan cilexetil, an angiotensin receptor blocker (ARB), indicated for the treatment of essential hypertension in adults and of adult patients with heart failure and impaired left ventricle systolic function (left ventricular ejection fraction ≤ 40%) as add-on therapy to Angiotensin Converting Enzyme (ACE inhibitors) or when ACE inhibitors are not tolerated.
This medicinal product was considered for SPC harmonisation and a referral was triggered in order to resolve divergences and harmonise the nationally authorised product information (PI) across Europe.
For the purpose of harmonisation, the CHMP considered the national PI, answers provided by the marketing authorisation holder (MAH) and available scientific knowledge.
A number of areas of disharmony were considered, in particular sections 4.1, 4.2, 4.3 and 4.4 of the summary of product characteristics (SPC). Other sections were also harmonised.

Section 4.1 Therapeutic indications

Hypertension indication
The hypertension indication was approved in all member states (MSs). The CHMP thus endorsed the wording "*Essential hypertension*".

Heart failure indication
The heart failure indication was approved in all MSs. However, the approved indication in one MS excluded patients falling in the New York Heart Association (NYHA) functional class IV.

The CHMP discussed the rational for this exclusion. Based on available data, including results from the CHARM study programme (Candesartan in Heart Failure: Assessment of Reduction in Mortality and morbidity) which included patients in NYHA functional class II to IV, the Committee noted there is no reason to exclude NYHA class IV patients. It is acknowledged that there is limited data in this population, however, analysis of the primary composite endpoint, cardiovascular death or hospitalisation due to heart failure by NYHA class subgroups in the low EF trials (CHARM-Alternative and CHARM-Added pooled, part of the CHARM programme), revealed Hazard Ratios (HR) below 1.0 in favour of candesartan compared to placebo in each of the NYHA subgroups.
In addition, there was no compelling indication that the results in any NYHA class subgroup were notably different from those described for the overall population. Moreover, there is no obvious biological reason for patients classified in NYHA class IV to respond differently to candesartan than other patients such as those classified to NYHA class III.
The CHMP considered that the benefit to risk ratio is positive also for patients in NYHA class IV and thus decided not to exclude these patients as recommended from the European Society of Cardiology (ESC).
The agreed indications were:

Atacand is indicated for the:
- *Treatment of essential hypertension in adults.*
- *Treatment of adult patients with heart failure and impaired left ventricular systolic function (left ventricular ejection fraction ≤ 40%) as add-on therapy to ACE inhibitors or when ACE inhibitors are not tolerated.*

Section 4.2 Posology and method of administration

Posology in hypertension
The recommended starting dose and usual maintenance dose of candesartan is 8 mg. In most of the MSs a dosage regimen up to a maximum of 32 mg dose was approved. The SPC in one MS mentioned the addition of a calcium channel blocker (CCB) as an additional alternative strategy.

The 32 mg dose is supported by study results in hypertensive patients and by a recently published dose-response analysis by *Karlson et al 2009*. Patients who respond with some reduction in blood pressure to candesartan monotherapy at lower doses may have further advantage of the full 32 mg dose. The recent ESH guidelines (*Mancia et al 2007*) and the Joint National Committee (JNC) VII guidelines (*Chobanian et al 2003*) for the treatment of hypertension state that the benefit may be substantial even when blood pressure reductions are small, and the initial blood pressure is below the traditional cut off defining hypertension. This is also confirmed in the recent meta-analysis by *Law et al* 2009, based on randomised trials.

Some studies support the addition of a calcium channel blocker (CCB), as additional strategy, (*Farsang et al* 2001, *Morgan and Anderson 2002* and *Lindholm et al 2003*). However, reference to an increased antihypertensive effect when candesartan cilexetil is combined with a CCB amlodipine or felodipine was not included in section 4.2 but rather in 5.1.

The CHMP considered that the available clinical data support a dose of candesartan up to 32 mg for the treatment of hypertension. A reference that candesartan can also be administrated with other antihypertensive agents was also included.

Sections on use in special populations, such as elderly, patients with intravascular volume depletion, patients with impaired renal and hepatic function and patients of black ethnicity were also harmonised. In the elderly, the CHMP considered that no initial dose adjustment was needed in patients over 75 years of age.
In patients with impaired hepatic function, the initial starting dose was changed from 2 mg to 4 mg. Results from two clinical studies investigating the pharmacokinetic (PK) profile of candesartan in patients with impaired hepatic function and the publication by *Hoogkamer et al 1998*, where a starting dose of 12 mg was used, indicate that mild to moderate hepatic impairment has no relevant effect on candesartan PK, and thus no dose adjustment is required. This conclusion was confirmed also in another study which looked at an even higher starting dose.

Posology in heart failure
The posology for patients with heart failure was the same in all MSs. The usual recommended initial dose of Atacand is 4 mg once daily. Up-titration to the target dose of 32 mg once daily (maximum dose) or the highest tolerated dose is done by doubling the dose at intervals of at least 2 weeks.

Regarding concomitant therapy, according to the ESC heart failure guidelines (ESC HF, 2008), the current standard of care in patients is an adequate dose of a beta-blocker and an ACE inhibitor. Should these agents be less than effective, addition of an ARB or a potassium sparing diuretic should be considered.
Results from the CHARM programme showed clear benefits with regard to cardiovascular (CV) mortality and morbidity for patients with heart failure on candesartan and concomitant medication. However, patients treated with candesartan, an ACE inhibitor and a potassium sparing diuretic experienced increased risk of hyperkalaemia. Patients who receive such combination therapy require careful and regular monitoring. The CHMP thus considered that although candesartan can be administered with other heart failure treatment (including ACE inhibitors, beta-blockers, diuretics and digitalis or a combination thereof), the association of an ACE inhibitor, a potassium-sparing diuretic and candesartan is not recommended.

Section 4.3 Contraindications

Pregnancy and lactation
A full contraindication in all trimesters of pregnancy and in lactation was previously included in the SPC.
However, the CHMP/PhVWP report on the use of ACE inhibitors and Angiotensin II Receptor Antagonists (ARBs) during the 1st trimester of pregnancy (EMEA/CHMP/PhVWP/474692/2007)

indicates that a contraindication during the first trimester of pregnancy is not justified; the use of AIIRAs in the first trimester of pregnancy is not recommended. The use of AIIRAs in the second and third trimester is contraindicated.

The CHMP also agreed with the inclusion of a contraindication in patients with hypersensitivity to candersartan or to any of its excipients and in patients with severe hepatic impairment and/or cholestasis.

Section 4.4 Special warnings and precautions for use

Warnings regarding renal impairment, concomitant therapy with an ACE inhibitor in heart failure, haemodialysis, renal artery stenosis, kidney transplantation, hypotension, anaesthesia and surgery, aortic and mitral valve stenosis, primary hyperaldosteronism and hyperkalaemia were harmonised. In line with the referred above, for heart failure patients treated with candesartan, hyperkalaemia may occur. Therefore, periodic monitoring of serum potassium is recommended and the combination of an ACE inhibitor, a potassium-sparing diuretic and candesartan is not recommended and should be considered only after careful evaluation of the potential benefits and risks.

Section 4.6 Pregnancy and Lactation

Based on the information provided, the CHMP endorsed the harmonised text for Angiotensin II receptor antagonists as the standard warning elaborated by the CHMP's Pharmacovigilance Working Party for all Angiotensin II receptor antagonists (AIIRAs): the use of AIIRAs in the first trimester of pregnancy is not recommended; the use of AIIRAs in the second and third trimester is contraindicated.

Section 4.7 Effects on Ability to Drive and Use Machines

The CHMP noted that there is plausible effect based on the pharmacologic action of the drug to affect the ability to drive thus this section was harmonised to reflect that '*dizziness'* and '*weariness'* can occur.

Section 4.8 Undesirable effects

The CHMP considered that the safety information in hypertension and chronic heart failure (CHF) should be presented separately. Additional wording separating the adverse events (AEs) findings from the CHARM programme was included as it illustrated that AE are more common in subjects who received other medicinal products which affect the renin-angiotensin system (RAS). In the Post-Marketing sub-section, the frequency "*Very Rare*" was replaced with the frequency "*not known*" as, for post marketing experience the frequency could not be estimated in accordance with the guideline on the SPC (September 2009).

Section 4.9 Overdose

The symptomatic manifestations of overdose and recommendations on management if it occurs were included in this section.

Section 5.1 Pharmacodynamic properties

This section was shortened and harmonised taking into account the current scientific knowledge and in line with the discussions for other sections of the SPC. In particular, updates on the potential dose increase up to 32 mg, increased antihypertensive effect when candesartan is combined with other medicinal products, including hydrochlorothiazide and CCB such as amlodipine or felodipine were considered. The presentation of results of a study in hypertension in the elderly was also harmonised. Regarding heart failure, the presentation of the results for the CHARM programme was harmonised.

Other sections of the SPC were harmonised accordingly.

Package leaflet and labelling
The changes to the SPC have been taken into account in the amendments to the PL and labelling as appropriate.

In conclusion, based on the assessment of the MAH proposal and responses, and following the discussions of the committee, the CHMP adopted harmonised sets of PI documents for Atacand and associated names. In particular, the indications and their associated posology recommendations, the contraindications and special warnings and precautions for use were harmonised.
Based on the above the CHMP considers the benefit/risk ratio of Atacand to be favourable and the harmonised PI to be approvable.

GROUNDS FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

Whereas

- the scope of the referral was the harmonisation of the Summary of Products Characteristics, labelling and package leaflet.

- the Summary of Products Characteristic, labelling and package leaflet proposed by the Marketing Authorisation Holders have been assessed based on the documentation submitted and the scientific discussion within the Committee,

the CHMP has recommended the amendment of the Marketing Authorisations for which the Summary of Product Characteristics, labelling and package leaflet are set out in Annex III for Atacand and associated names (see Annex I).

ANNEX III

**SUMMARY OF PRODUCT CHARACTERISTICS,
LABELLING AND PACKAGE LEAFLET**

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Atacand and associated names (see Annex I) 2 mg tablets
Atacand and associated names (see Annex I) 4 mg tablets
Atacand and associated names (see Annex I) 8 mg tablets
Atacand and associated names (see Annex I) 16 mg tablets
Atacand and associated names (see Annex I) 32 mg tablets

[See Annex I - To be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[To be completed nationally]

3. PHARMACEUTICAL FORM

Tablet

[To be completed nationally]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Atacand is indicated for the:

- Treatment of essential hypertension in adults.
- Treatment of adult patients with heart failure and impaired left ventricular systolic function (left ventricular ejection fraction ≤ 40%) as add-on therapy to Angiotensin Converting Enzyme (ACE) inhibitors or when ACE inhibitors are not tolerated (see section 5.1).

4.2 Posology and method of administration

Posology in Hypertension

The recommended initial dose and usual maintenance dose of Atacand is 8 mg once daily. Most of the antihypertensive effect is attained within 4 weeks. In some patients whose blood pressure is not adequately controlled, the dose can be increased to 16 mg once daily and to a maximum of 32 mg once daily. Therapy should be adjusted according to blood pressure response.
Atacand may also be administered with other antihypertensive agents. Addition of hydrochlorothiazide has been shown to have an additive antihypertensive effect with various doses of Atacand.

Elderly population
No initial dose adjustment is necessary in elderly patients.

Patients with intravascular volume depletion
An initial dose of 4 mg may be considered in patients at risk for hypotension, such as patients with possible volume depletion (see section 4.4).

Patients with renal impairment
The starting dose is 4 mg in patients with renal impairment, including patients on haemodialysis. The dose should be titrated according to response. There is limited experience in patients with very severe or end-stage renal impairment ($Cl_{creatinine}$ < 15 ml/min) (see section 4.4).

Patients with hepatic impairment
An initial dose of 4 mg once daily is recommended in patients with mild to moderate hepatic impairment. The dose may be adjusted according to response. Atacand is contraindicated in patients with severe hepatic impairment and/or cholestasis (see sections 4.3 and 5.2).

Black patients
The antihypertensive effect of candesartan is less pronounced in black patients than in non-black patients. Consequently, uptitration of Atacand and concomitant therapy may be more frequently needed for blood pressure control in black patients than in non-black patients (see section 5.1).

Posology in Heart Failure

The usual recommended initial dose of Atacand is 4 mg once daily. Up-titration to the target dose of 32 mg once daily (maximum dose) or the highest tolerated dose is done by doubling the dose at intervals of at least 2 weeks (see section 4.4). Evaluation of patients with heart failure should always comprise assessment of renal function including monitoring of serum creatinine and potassium. Atacand can be administered with other heart failure treatment, including ACE inhibitors, beta-blockers, diuretics and digitalis or a combination of these medicinal products. The combination of an ACE inhibitor, a potassium-sparing diuretic (e.g. spironolactone) and Atacand is not recommended and should be considered only after careful evaluation of the potential benefits and risks (see sections 4.4, 4.8 and 5.1).

Special patient populations
No initial dose adjustment is necessary for elderly patients or in patients with intravascular volume depletion or renal impairment or mild to moderate hepatic impairment.

Paediatric Population

The safety and efficacy of Atacand in children aged between birth and 18 years have not been established in the treatment of hypertension and heart failure. No data are available.

Method of administration

Oral use.
Atacand should be taken once daily with or without food.
The bioavailability of candesartan is not affected by food.

4.3 Contraindications

Hypersensitivity to candesartan cilexetil or to any of the excipients.
Second and third trimesters of pregnancy (see sections 4.4 and 4.6).
Severe hepatic impairment and/or cholestasis.

4.4 Special warnings and precautions for use

Renal impairment
As with other agents inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible patients treated with Atacand.

When Atacand is used in hypertensive patients with renal impairment, periodic monitoring of serum potassium and creatinine levels is recommended. There is limited experience in patients with very severe or end-stage renal impairment ($Cl_{creatinine}$ < 15 ml/min). In these patients Atacand should be carefully titrated with thorough monitoring of blood pressure.

Evaluation of patients with heart failure should include periodic assessments of renal function, especially in elderly patients 75 years or older, and patients with impaired renal function. During dose titration of Atacand, monitoring of serum creatinine and potassium is recommended. Clinical trials in heart failure did not include patients with serum creatinine > 265 μmol/l (> 3 mg/dl).

Concomitant therapy with an ACE inhibitor in heart failure
The risk of adverse reactions, especially renal function impairment and hyperkalaemia, may increase when Atacand is used in combination with an ACE inhibitor (see section 4.8). Patients with such treatment should be monitored regularly and carefully.

Haemodialysis
During dialysis the blood pressure may be particularly sensitive to AT_1-receptor blockade as a result of reduced plasma volume and activation of the renin-angiotensin-aldosterone system. Therefore, Atacand should be carefully titrated with thorough monitoring of blood pressure in patients on haemodialysis.

Renal artery stenosis
Medicinal products that affect the renin-angiotensin-aldosterone system, including angiotensin II receptor antagonists (AIIRAs), may increase blood urea and serum creatinine in patients with bilateral renal artery stenosis or stenosis of the artery to a solitary kidney.

Kidney transplantation
There is no experience regarding the administration of Atacand in patients with a recent kidney transplantation.

Hypotension
Hypotension may occur during treatment with Atacand in heart failure patients. It may also occur in hypertensive patients with intravascular volume depletion such as those receiving high dose diuretics. Caution should be observed when initiating therapy and correction of hypovolemia should be attempted.

Anaesthesia and surgery
Hypotension may occur during anaesthesia and surgery in patients treated with angiotensin II antagonists due to blockade of the renin-angiotensin system. Very rarely, hypotension may be severe such that it may warrant the use of intravenous fluids and/or vasopressors.

Aortic and mitral valve stenosis (obstructive hypertrophic cardiomyopathy)
As with other vasodilators, special caution is indicated in patients suffering from haemodynamically relevant aortic or mitral valve stenosis, or obstructive hypertrophic cardiomyopathy.

Primary hyperaldosteronism
Patients with primary hyperaldosteronism will not generally respond to antihypertensive medicinal products acting through inhibition of the renin-angiotensin-aldosterone system. Therefore, the use of Atacand is not recommended in this population.

Hyperkalaemia
Concomitant use of Atacand with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, or other medicinal products that may increase potassium levels (e.g. heparin) may lead to increases in serum potassium in hypertensive patients. Monitoring of potassium should be undertaken as appropriate.

In heart failure patients treated with Atacand, hyperkalaemia may occur. Periodic monitoring of serum potassium is recommended. The combination of an ACE inhibitor, a potassium-sparing diuretic (e.g. spironolactone) and Atacand is not recommended and should be considered only after careful evaluation of the potential benefits and risks.

General
In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with other medicinal products that affect this system has been associated with acute hypotension, azotaemia, oliguria or, rarely, acute renal failure. The possibility of similar effects cannot be excluded with AIIRAs. As with any antihypertensive agent, excessive blood pressure decrease in patients with ischaemic cardiopathy or ischaemic cerebrovascular disease could result in a myocardial infarction or stroke.

The antihypertensive effect of candesartan may be enhanced by other medicinal products with blood pressure lowering properties, whether prescribed as an antihypertensive or prescribed for other indications.

Atacand contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Pregnancy
AIIRAs should not be initiated during pregnancy. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately, and, if appropriate, alternative therapy should be started (see sections 4.3 and 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

Compounds which have been investigated in clinical pharmacokinetic studies include hydrochlorothiazide, warfarin, digoxin, oral contraceptives (i.e. ethinylestradiol/levonorgestrel), glibenclamide, nifedipine and enalapril. No clinically significant pharmacokinetic interactions with these medicinal products have been identified.

Concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, or other medicinal products (e.g. heparin) may increase potassium levels. Monitoring of potassium should be undertaken as appropriate (see section 4.4).

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ACE inhibitors. A similar effect may occur with AIIRAs. Use of candesartan with lithium is not recommended. If the combination proves necessary, careful monitoring of serum lithium levels is recommended.

When AIIRAs are administered simultaneously with non-steroidal anti-inflammatory drugs (NSAIDs) (i.e. selective COX-2 inhibitors, acetylsalicylic acid (> 3 g/day) and non-selective NSAIDs), attenuation of the antihypertensive effect may occur.

As with ACE inhibitors, concomitant use of AIIRAs and NSAIDs may lead to an increased risk of worsening of renal function, including possible acute renal failure, and an increase in serum potassium, especially in patients with poor pre-existing renal function. The combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring renal function after initiation of concomitant therapy, and periodically thereafter.

4.6 Pregnancy and lactation

Pregnancy

The use of AIIRAs is not recommended during the first trimester of pregnancy (see section 4.4). The use of AIIRAs is contraindicated during the second and third trimesters of pregnancy (see sections 4.3 and 4.4).

Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE inhibitors during the first trimester of pregnancy has not been conclusive; however a small increase in risk cannot be excluded. Whilst there is no controlled epidemiological data on the risk with AIIRAs, similar risks may exist for this class of drugs. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately and, if appropriate, alternative therapy should be started.

Exposure to AIIRA therapy during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia) (see section 5.3).
Should exposure to AIIRAs have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended.
Infants whose mothers have taken AIIRAs should be closely observed for hypotension (see sections 4.3 and 4.4).

Lactation

Because no information is available regarding the use of Atacand during breastfeeding, Atacand is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.

4.7 Effects on ability to drive and use machines

No studies on the effects of candesartan on the ability to drive and use machines have been performed. However, it should be taken into account that occasionally dizziness or weariness may occur during treatment with Atacand.

4.8 Undesirable effects

Treatment of Hypertension

In controlled clinical studies adverse reactions were mild and transient. The overall incidence of adverse events showed no association with dose or age. Withdrawals from treatment due to adverse events were similar with candesartan cilexetil (3.1%) and placebo (3.2%).

In a pooled analysis of clinical trial data of hypertensive patients, adverse reactions with candesartan cilexetil were defined based on an incidence of adverse events with candesartan cilexetil at least 1% higher than the incidence seen with placebo. By this definition, the most commonly reported adverse reactions were dizziness/vertigo, headache and respiratory infection.

The table below presents adverse reactions from clinical trials and post-marketing experience.

The frequencies used in the tables throughout section 4.8 are: 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).

System Organ Class	Frequency	Undesirable Effect
Infections and infestations	Common	Respiratory infection
Blood and lymphatic system disorders	Very rare	Leukopenia, neutropenia and agranulocytosis

System Organ Class	Frequency	Undesirable Effect
Metabolism and nutrition disorders	Very rare	Hyperkalaemia, hyponatraemia
Nervous system disorders	Common	Dizziness/vertigo, headache
Gastrointestinal disorders	Very rare	Nausea
Hepato-biliary disorders	Very rare	Increased liver enzymes, abnormal hepatic function or hepatitis
Skin and subcutaneous tissue disorders	Very rare	Angioedema, rash, urticaria, pruritus
Musculoskeletal and connective tissue disorders	Very rare	Back pain, arthralgia, myalgia
Renal and urinary disorders	Very rare	Renal impairment, including renal failure in susceptible patients (see section 4.4)

Laboratory findings
In general, there were no clinically important influences of Atacand on routine laboratory variables. As for other inhibitors of the renin-angiotensin-aldosterone system, small decreases in haemoglobin have been seen. No routine monitoring of laboratory variables is usually necessary for patients receiving Atacand. However, in patients with renal impairment, periodic monitoring of serum potassium and creatinine levels is recommended.

Treatment of Heart Failure

The adverse experience profile of Atacand in heart failure patients was consistent with the pharmacology of the drug and the health status of the patients. In the CHARM clinical programme, comparing Atacand in doses up to 32 mg (n=3,803) to placebo (n=3,796), 21.0% of the candesartan cilexetil group and 16.1% of the placebo group discontinued treatment because of adverse events. The most commonly reported adverse reactions were hyperkalaemia, hypotension and renal impairment. These events were more common in patients over 70 years of age, diabetics, or subjects who received other medicinal products which affect the renin-angiotensin-aldosterone system, in particular an ACE inhibitor and/or spironolactone.

The table below presents adverse reactions from clinical trials and post-marketing experience.

System Organ Class	Frequency	Undesirable Effect
Blood and lymphatic system disorders	Very rare	Leukopenia, neutropenia and agranulocytosis
Metabolism and nutrition disorders	Common	Hyperkalaemia
	Very rare	Hyponatraemia
Nervous system disorders	Very rare	Dizziness, headache
Vascular disorders	Common	Hypotension
Gastrointestinal disorders	Very rare	Nausea
Hepato-biliary disorders	Very rare	Increased liver enzymes, abnormal hepatic function or hepatitis
Skin and subcutaneous tissue disorders	Very rare	Angioedema, rash, urticaria, pruritus
Musculoskeletal and connective tissue disorders	Very rare	Back pain, arthralgia, myalgia
Renal and urinary disorders	Common	Renal impairment, including renal failure in susceptible patients (see section 4.4)

Laboratory findings

Hyperkalaemia and renal impairment are common in patients treated with Atacand for the indication of heart failure. Periodic monitoring of serum creatinine and potassium is recommended (see section 4.4).

4.9 Overdose

Symptoms

Based on pharmacological considerations, the main manifestation of an overdose is likely to be symptomatic hypotension and dizziness. In individual case reports of overdose (of up to 672 mg candesartan cilexetil) patient recovery was uneventful.

Management

If symptomatic hypotension should occur, symptomatic treatment should be instituted and vital signs monitored. The patient should be placed supine with the legs elevated. If this is not sufficient, plasma volume should be increased by infusion of, for example, isotonic saline solution. Sympathomimetic medicinal products may be administered if the above-mentioned measures are not sufficient. Candesartan is not removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
Angiotensin II antagonists, plain, ATC code: C09CA06

Angiotensin II is the primary vasoactive hormone of the renin-angiotensin-aldosterone system and plays a role in the pathophysiology of hypertension, heart failure and other cardiovascular disorders. It also has a role in the pathogenesis of end organ hypertrophy and damage. The major physiological effects of angiotensin II, such as vasoconstriction, aldosterone stimulation, regulation of salt and water homeostasis and stimulation of cell growth, are mediated via the type 1 (AT_1) receptor.

Candesartan cilexetil is a prodrug suitable for oral use. It is rapidly converted to the active substance, candesartan, by ester hydrolysis during absorption from the gastrointestinal tract. Candesartan is an AIIRA, selective for AT_1 receptors, with tight binding to and slow dissociation from the receptor. It has no agonist activity.

Candesartan does not inhibit ACE, which converts angiotensin I to angiotensin II and degrades bradykinin. There is no effect on ACE and no potentiation of bradykinin or substance P. In controlled clinical trials comparing candesartan with ACE inhibitors, the incidence of cough was lower in patients receiving candesartan cilexetil. Candesartan does not bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation. The antagonism of the angiotensin II (AT_1) receptors results in dose related increases in plasma renin levels, angiotensin I and angiotensin II levels, and a decrease in plasma aldosterone concentration.

Hypertension

In hypertension, candesartan causes a dose-dependent, long-lasting reduction in arterial blood pressure. The antihypertensive action is due to decreased systemic peripheral resistance, without reflex increase in heart rate. There is no indication of serious or exaggerated first dose hypotension or rebound effect after cessation of treatment.

After administration of a single dose of candesartan cilexetil, onset of antihypertensive effect generally occurs within 2 hours. With continuous treatment, most of the reduction in blood pressure with any dose is generally attained within four weeks and is sustained during long-term treatment. According to

a meta-analysis, the average additional effect of a dose increase from 16 mg to 32 mg once daily was small. Taking into account the inter-individual variability, a more than average effect can be expected in some patients. Candesartan cilexetil once daily provides effective and smooth blood pressure reduction over 24 hours, with little difference between maximum and trough effects during the dosing interval. The antihypertensive effect and tolerability of candesartan and losartan were compared in two randomised, double-blind studies in a total of 1,268 patients with mild to moderate hypertension. The trough blood pressure reduction (systolic/diastolic) was 13.1/10.5 mmHg with candesartan cilexetil 32 mg once daily and 10.0/8.7 mmHg with losartan potassium 100 mg once daily (difference in blood pressure reduction 3.1/1.8 mmHg, $p<0.0001/p<0.0001$).

When candesartan cilexetil is used together with hydrochlorothiazide, the reduction in blood pressure is additive. An increased antihypertensive effect is also seen when candesartan cilexetil is combined with amlodipine or felodipine.

Medicinal products that block the renin-angiotensin-aldosterone system have less pronounced antihypertensive effect in black patients (usually a low-renin population) than in non-black patients. This is also the case for candesartan. In an open label clinical experience trial in 5,156 patients with diastolic hypertension, the blood pressure reduction during candesartan treatment was significantly less in black than non-black patients (14.4/10.3 mmHg vs 19.0/12.7 mmHg, $p<0.0001/p<0.0001$).

Candesartan increases renal blood flow and either has no effect on or increases glomerular filtration rate while renal vascular resistance and filtration fraction are reduced. In a 3-month clinical study in hypertensive patients with type 2 diabetes mellitus and microalbuminuria, antihypertensive treatment with candesartan cilexetil reduced urinary albumin excretion (albumin/creatinine ratio, mean 30%, 95%CI 15-42%). There is currently no data on the effect of candesartan on the progression to diabetic nephropathy.

The effects of candesartan cilexetil 8-16 mg (mean dose 12 mg), once daily, on cardiovascular morbidity and mortality were evaluated in a randomised clinical trial with 4,937 elderly patients (aged 70-89 years; 21% aged 80 or above) with mild to moderate hypertension followed for a mean of 3.7 years (Study on COgnition and Prognosis in the Elderly). Patients received candesartan cilexetil or placebo with other antihypertensive treatment added as needed. The blood pressure was reduced from 166/90 to 145/80 mmHg in the candesartan group, and from 167/90 to 149/82 mmHg in the control group. There was no statistically significant difference in the primary endpoint, major cardiovascular events (cardiovascular mortality, non-fatal stroke and non-fatal myocardial infarction). There were 26.7 events per 1000 patient-years in the candesartan group versus 30.0 events per 1000 patient-years in the control group (relative risk 0.89, 95%CI 0.75 to 1.06, p=0.19).

Heart Failure

Treatment with candesartan cilexetil reduces mortality, reduces hospitalisation due to heart failure, and improves symptoms in patients with left ventricular systolic dysfunction as shown in the Candesartan in Heart failure – Assessment of Reduction in Mortality and morbidity (CHARM) programme.

This placebo controlled, double-blind study programme in chronic heart failure (CHF) patients with NYHA functional class II to IV consisted of three separate studies: CHARM-Alternative (n=2,028) in patients with LVEF ≤ 40% not treated with an ACE inhibitor because of intolerance (mainly due to cough, 72%), CHARM-Added (n=2,548) in patients with LVEF ≤ 40% and treated with an ACE inhibitor, and CHARM-Preserved (n=3,023) in patients with LVEF > 40%. Patients on optimal CHF therapy at baseline were randomised to placebo or candesartan cilexetil (titrated from 4 mg or 8 mg once daily to 32 mg once daily or the highest tolerated dose, mean dose 24 mg) and followed for a median of 37.7 months. After 6 months of treatment 63% of the patients still taking candesartan cilexetil (89%) were at the target dose of 32 mg.

In CHARM-Alternative, the composite endpoint of cardiovascular mortality or first CHF hospitalisation was significantly reduced with candesartan in comparison with placebo, hazard ratio (HR) 0.77 (95%CI: 0.67 to 0.89, p< 0.001). This corresponds to a relative risk reduction of 23%. Of

candesartan patients 33.0% (95%CI: 30.1 to 36.0) and of placebo patients 40.0% (95%CI: 37.0 to 43.1) experienced this endpoint, absolute difference 7.0% (95%CI: 11.2 to 2.8). Fourteen patients needed to be treated for the duration of the study to prevent one patient from dying of a cardiovascular event or being hospitalised for treatment of heart failure. The composite endpoint of all-cause mortality or first CHF hospitalisation was also significantly reduced with candesartan, HR 0.80 (95%CI: 0.70 to 0.92, p=0.001). Of candesartan patients 36.6% (95%CI: 33.7 to 39.7) and of placebo patients 42.7% (95%CI: 39.6 to 45.8) experienced this endpoint, absolute difference 6.0% (95%CI: 10.3 to 1.8). Both the mortality and morbidity (CHF hospitalisation) components of these composite endpoints contributed to the favourable effects of candesartan. Treatment with candesartan cilexetil resulted in improved NYHA functional class (p=0.008).

In CHARM-Added, the composite endpoint of cardiovascular mortality or first CHF hospitalisation was significantly reduced with candesartan in comparison with placebo, HR 0.85 (95%CI: 0.75 to 0.96, p=0.011). This corresponds to a relative risk reduction of 15%. Of candesartan patients 37.9% (95%CI: 35.2 to 40.6) and of placebo patients 42.3% (95%CI: 39.6 to 45.1) experienced this endpoint, absolute difference 4.4% (95%CI: 8.2 to 0.6). Twenty-three patients needed to be treated for the duration of the study to prevent one patient from dying of a cardiovascular event or being hospitalised for treatment of heart failure. The composite endpoint of all-cause mortality or first CHF hospitalisation was also significantly reduced with candesartan, HR 0.87 (95%CI: 0.78 to 0.98, p=0.021). Of candesartan patients 42.2% (95%CI: 39.5 to 45.0) and of placebo patients 46.1% (95%CI: 43.4 to 48.9) experienced this endpoint, absolute difference 3.9% (95%CI: 7.8 to 0.1). Both the mortality and morbidity components of these composite endpoints contributed to the favourable effects of candesartan. Treatment with candesartan cilexetil resulted in improved NYHA functional class (p=0.020).

In CHARM-Preserved, no statistically significant reduction was achieved in the composite endpoint of cardiovascular mortality or first CHF hospitalisation, HR 0.89 (95%CI: 0.77 to 1.03, p=0.118).

All-cause mortality was not statistically significant when examined separately in each of the three CHARM studies. However, all-cause mortality was also assessed in pooled populations, CHARM-Alternative and CHARM-Added, HR 0.88 (95%CI: 0.79 to 0.98, p=0.018) and all three studies, HR 0.91 (95%CI: 0.83 to 1.00, p=0.055).

The beneficial effects of candesartan were consistent irrespective of age, gender and concomitant medication. Candesartan was effective also in patients taking both beta-blockers and ACE inhibitors at the same time, and the benefit was obtained whether or not patients were taking ACE inhibitors at the target dose recommended by treatment guidelines.

In patients with CHF and depressed left ventricular systolic function (left ventricular ejection fraction, LVEF ≤ 40%), candesartan decreases systemic vascular resistance and pulmonary capillary wedge pressure, increases plasma renin activity and angiotensin II concentration, and decreases aldosterone levels.

5.2 Pharmacokinetic properties

Absorption and distribution

Following oral administration, candesartan cilexetil is converted to the active substance candesartan. The absolute bioavailability of candesartan is approximately 40% after an oral solution of candesartan cilexetil. The relative bioavailability of the tablet formulation compared with the same oral solution is approximately 34% with very little variability. The estimated absolute bioavailability of the tablet is therefore 14%. The mean peak serum concentration (C_{max}) is reached 3-4 hours following tablet intake. The candesartan serum concentrations increase linearly with increasing doses in the therapeutic dose range. No gender related differences in the pharmacokinetics of candesartan have been observed. The area under the serum concentration *versus* time curve (AUC) of candesartan is not significantly affected by food.

Candesartan is highly bound to plasma protein (more than 99%). The apparent volume of distribution of candesartan is 0.1 l/kg.

The bioavailability of candesartan is not affected by food.

Biotransformation and elimination

Candesartan is mainly eliminated unchanged via urine and bile and only to a minor extent eliminated by hepatic metabolism (CYP2C9). Available interaction studies indicate no effect on CYP2C9 and CYP3A4. Based on *in vitro* data, no interaction would be expected to occur *in vivo* with drugs whose metabolism is dependent upon cytochrome P450 isoenzymes CYP1A2, CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP2E1 or CYP3A4. The terminal half-life of candesartan is approximately 9 hours. There is no accumulation following multiple doses.

Total plasma clearance of candesartan is about 0.37 ml/min/kg, with a renal clearance of about 0.19 ml/min/kg. The renal elimination of candesartan is both by glomerular filtration and active tubular secretion. Following an oral dose of ^{14}C-labelled candesartan cilexetil, approximately 26% of the dose is excreted in the urine as candesartan and 7% as an inactive metabolite while approximately 56% of the dose is recovered in the faeces as candesartan and 10% as the inactive metabolite.

Pharmacokinetics in special populations

In the elderly (over 65 years) C_{max} and AUC of candesartan are increased by approximately 50% and 80%, respectively in comparison to young subjects. However, the blood pressure response and the incidence of adverse events are similar after a given dose of Atacand in young and elderly patients (see section 4.2).

In patients with mild to moderate renal impairment C_{max} and AUC of candesartan increased during repeated dosing by approximately 50% and 70%, respectively, but $t_{½}$ was not altered, compared to patients with normal renal function. The corresponding changes in patients with severe renal impairment were approximately 50% and 110%, respectively. The terminal $t_{½}$ of candesartan was approximately doubled in patients with severe renal impairment. The AUC of candesartan in patients undergoing haemodialysis was similar to that in patients with severe renal impairment.

In two studies, both including patients with mild to moderate hepatic impairment, there was an increase in the mean AUC of candesartan of approximately 20% in one study and 80% in the other study (see section 4.2). There is no experience in patients with severe hepatic impairment.

5.3 Preclinical safety data

There was no evidence of abnormal systemic or target organ toxicity at clinically relevant doses. In preclinical safety studies candesartan had effects on the kidneys and on red cell parameters at high doses in mice, rats, dogs and monkeys. Candesartan caused a reduction of red blood cell parameters (erythrocytes, haemoglobin, haematocrit). Effects on the kidneys (such as interstitial nephritis, tubular distension, basophilic tubules; increased plasma concentrations of urea and creatinine) were induced by candesartan which could be secondary to the hypotensive effect leading to alterations of renal perfusion. Furthermore, candesartan induced hyperplasia/hypertrophy of the juxtaglomerular cells. These changes were considered to be caused by the pharmacological action of candesartan. For therapeutic doses of candesartan in humans, the hyperplasia/hypertrophy of the renal juxtaglomerular cells does not seem to have any relevance.

Foetotoxicity has been observed in late pregnancy (see section 4.6).

Data from *in vitro* and *in vivo* mutagenicity testing indicates that candesartan will not exert mutagenic or clastogenic activities under conditions of clinical use.

There was no evidence of carcinogenicity.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[To be completed nationally]

6.2 Incompatibilities

[To be completed nationally]

6.3 Shelf life

[To be completed nationally]

6.4 Special precautions for storage

[To be completed nationally]

6.5 Nature and contents of container

[To be completed nationally]

6.6 Special precautions for disposal and other handling

No special requirements

7. MARKETING AUTHORISATION HOLDER

[See Annex I - to be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

[To be completed nationally]

Detailed information on this product is available on the website of : {name of MS/Agency}

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON FOR BLISTER / CARTON FOR BOTTLE / LABEL FOR BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

Atacand and associated names (see Annex I) 2 mg tablets
Atacand and associated names (see Annex I) 4 mg tablets
Atacand and associated names (see Annex I) 8 mg tablets
Atacand and associated names (see Annex I) 16 mg tablets
Atacand and associated names (see Annex I) 32 mg tablets

[See Annex I - To be completed nationally]

candesartan cilexetil

2. STATEMENT OF ACTIVE SUBSTANCE(S)

[To be completed nationally]

3. LIST OF EXCIPIENTS

Contains lactose. See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

[To be completed nationally]

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 REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

[To be completed nationally]

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

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS

Non-Perforated foil, Perforated foil

1. NAME OF THE MEDICINAL PRODUCT

Atacand and associated names (see Annex I) 2 mg tablets
Atacand and associated names (see Annex I) 4 mg tablets
Atacand and associated names (see Annex I) 8 mg tablets
Atacand and associated names (see Annex I) 16 mg tablets
Atacand and associated names (see Annex I) 32 mg tablets

[See Annex I - To be completed nationally]

candesartan cilexetil

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

MINIMUM PARTICULARS TO APPEAR ON BLISTERS

Non-Perforated calendar foil (7, 14, 28, 56 and 98 tablets)

1. NAME OF THE MEDICINAL PRODUCT

Atacand and associated names (see Annex I) 2 mg tablets
Atacand and associated names (see Annex I) 4 mg tablets
Atacand and associated names (see Annex I) 8 mg tablets
Atacand and associated names (see Annex I) 16 mg tablets
Atacand and associated names (see Annex I) 32 mg tablets

[See Annex I - To be completed nationally]

candesartan cilexetil

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Mon Tue Wed Thur Fri Sat Sun

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Atacand and associated names (see Annex I) 2 mg tablets
Atacand and associated names (see Annex I) 4 mg tablets
Atacand and associated names (see Annex I) 8 mg tablets
Atacand and associated names (see Annex I) 16 mg tablets
Atacand and associated names (see Annex I) 32 mg tablets

[See Annex I - To be completed nationally]

candesartan cilexetil

Read all of this leaflet carefully before you start taking this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT ATACAND IS AND WHAT IT IS USED FOR

The name of your medicine is Atacand. The active ingredient is candesartan cilexetil. This belongs to a group of medicines called angiotensin II receptor antagonists. It works by making your blood vessels relax and widen. This helps to lower your blood pressure. It also makes it easier for your heart to pump blood to all parts of your body.

This is medicine is used for:
- treating high blood pressure (hypertension) in adult patients.
- treating adult heart failure patients with reduced heart muscle function, in addition to Angiotensin Converting Enzyme (ACE) inhibitors or when ACE inhibitors cannot be used (ACE inhibitors are a group of medicines used to treat heart failure).

2. BEFORE YOU TAKE ATACAND

Do not take Atacand
- if you are allergic (hypersensitive) to candesartan cilexetil or any of the other ingredients of Atacand (see section 6).
- if you are more than 3 months pregnant (it is also better to avoid Atacand in early pregnancy – see pregnancy section).
- if you have severe liver disease or biliary obstruction (a problem with the drainage of the bile from the gall bladder).

If you are not sure if any of these apply to you, talk to your doctor or pharmacist before taking Atacand.

Take special care with Atacand

Before you take, or whilst you are taking Atacand, tell your doctor.

- if you have heart, liver or kidney problems, or are on dialysis.
- if you have recently had a kidney transplant.
- if you are vomiting, have recently had severe vomiting, or have diarrhoea.
- if you have a disease of the adrenal gland called Conn's syndrome (also called primary hyperaldosteronism).
- if you have low blood pressure.
- if you have ever had a stroke.
- you must tell your doctor if you think you are (or might become) pregnant. Atacand is not recommended in early pregnancy, and must not be taken if you are more than 3 months pregnant, as it may cause serious harm to your baby if used at that stage (see pregnancy section).

Your doctor may want to see you more often and do some tests if you have any of these conditions.

If you are going to have an operation, tell your doctor or dentist that you are taking Atacand. This is because Atacand, when combined with some anaesthetics, may cause a drop in blood pressure.

Use in children
There is no experience with the use of Atacand in children (below the age of 18 years). Therefore Atacand should not be given to children.

Using other medicines
Please tell your doctor or pharmacist if you are using, or have recently used, any other medicines, including medicines obtained without a prescription.
Atacand can affect the way some other medicines work and some medicines can have an effect on Atacand. If you are using certain medicines, your doctor may need to do blood tests from time to time.

In particular, tell your doctor if you are using any of the following medicines:

- Other medicines to help lower your blood pressure, including beta-blockers, diazoxide and ACE inhibitors such as enalapril, captopril, lisinopril or ramipril.
- Non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen, naproxen, diclofenac, celecoxib or etoricoxib (medicines to relieve pain and inflammation).
- Acetylsalicylic acid (if you are taking more than 3 g each day) (medicine to relieve pain and inflammation).
- Potassium supplements or salt substitutes containing potassium (medicines that increase the amount of potassium in your blood).
- Heparin (a medicine for thinning the blood).
- Water tablets (diuretics).
- Lithium (a medicine for mental health problems).

Taking Atacand with food and drink (in particular alcohol)

- You can take Atacand with or without food.
- When you are prescribed Atacand, discuss with your doctor before drinking alcohol. Alcohol may make you feel faint or dizzy.

Pregnancy and breast-feeding

Pregnancy
You must tell your doctor if you think you are (or might become) pregnant. Your doctor will normally advise you to stop taking Atacand before you become pregnant or as soon as you know you are pregnant and will advise you to take another medicine instead of Atacand. Atacand is not recommended in early pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy.

Breast-feeding
Tell your doctor if you are breast-feeding or about to start breast-feeding. Atacand is not recommended for mothers who are breast-feeding, and your doctor may choose another treatment for you if you wish to breast-feed, especially if your baby is newborn, or was born prematurely.

Driving and using machines
Some people may feel tired or dizzy when taking Atacand. If this happens to you, do not drive or use any tools or machines.

Important information about some of the ingredients of Atacand
Atacand contains lactose which is a type of sugar. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. HOW TO TAKE ATACAND

Always take Atacand exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure. It is important to keep taking Atacand every day.
You can take Atacand with or without food.
Swallow the tablet with a drink of water.
Try to take the tablet at the same time each day. This will help you to remember to take it.

High blood pressure:
- The usual dose of Atacand is 8 mg once a day. Your doctor may increase this dose to 16 mg once a day and further up to 32 mg once a day depending on blood pressure response.
- In some patients, such as those with liver problems, kidney problems or those who recently have lost body fluids, e.g., through vomiting or diarrhoea or by using water tablets, the doctor may prescribe a lower starting dose.
- Some black patients may have a reduced response to this type of medicine, when given as the only treatment, and these patients may need a higher dose.

Heart failure:
- The usual starting dose of Atacand is 4 mg once a day. Your doctor may increase your dose by doubling the dose at intervals of at least 2 weeks up to 32 mg once a day. Atacand can be taken together with other medicines for heart failure, and your doctor will decide which treatment is suitable for you.

If you take more Atacand than you should
If you take more Atacand than prescribed by your doctor, contact a doctor or pharmacist immediately for advice.

If you forget to take Atacand
Do not take a double dose to make up for a forgotten tablet. Just take the next dose as normal.

If you stop taking Atacand
If you stop taking Atacand, your blood pressure may increase again. Therefore do not stop taking Atacand without first talking to your doctor.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Atacand can cause side effects, although not everybody gets them. It is important that you are aware of what these side effects may be.

Stop taking Atacand and seek medical help immediately if you have any of the following allergic reactions:
- difficulties in breathing, with or without swelling of the face, lips, tongue and/or throat
- swelling of the face, lips, tongue and/or throat, which may cause difficulties in swallowing
- severe itching of the skin (with raised lumps)

Atacand may cause a reduction in number of white blood cells. Your resistance to infection may be decreased and you may notice tiredness, an infection or a fever. If this happens contact your doctor. Your doctor may occasionally do blood tests to check whether Atacand has had any effect on your blood (agranulocytosis).

Other possible side effects include:
Common (affects 1 to 10 users in 100)
- Feeling dizzy/spinning sensation.
- Headache.
- Respiratory infection.
- Low blood pressure. This may make you feel faint or dizzy.
- Changes in blood test results:
  - An increased amount of potassium in your blood, especially if you already have kidney problems or heart failure. If this is severe you may notice tiredness, weakness, irregular heart beat or pins and needles.
- Effects on how your kidneys work, especially if you already have kidney problems or heart failure. In very rare cases, kidney failure may occur.

Very rare (affects less than 1 user in 10,000)
- Swelling of the face, lips, tongue and/or throat.
- A reduction in your red or white blood cells. You may notice tiredness, an infection or a fever.
- Skin rash, lumpy rash (hives).
- Itching.
- Back pain, pain in joints and muscles.
- Changes in how your liver is working, including inflammation of the liver (hepatitis). You may notice tiredness, yellowing of your skin and the whites of your eyes and flu like symptoms.
- Nausea.
- Changes in blood test results:
  - A reduced amount of sodium in your blood. If this is severe then you may notice weakness, lack of energy, or muscle cramps.

If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE ATACAND

[To be completed nationally]

- Keep out of the reach and sight of children.
- Do not use Atacand after the expiry date which is stated on the carton, blister pack or bottle. The expiry date refers to the last day of that month.
- This medicinal product does not require any special temperature storage conditions.

Medicines should not be disposed of 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. FURTHER INFORMATION

What Atacand contains

[To be completed nationally]

What Atacand looks like and contents of the pack

[To be completed nationally]

Marketing Authorisation Holder and Manufacturer

[See Annex I - To be completed nationally]

{Name and address of the manufacturer}
<{tel}>
<{fax}>
<{e-mail}>

This medicinal product is authorised in the Member States of the EEA under the following names:

Member State	Name
Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Malta, The Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, UK	Atacand
Italy	Ratacand
Sweden	Racanda

This leaflet was last approved in {MM/YYYY}.

[To be completed nationally]