ANNEX I

LIST OF THE NAMES, PHARMACEUTICAL FORMS, STRENGTHS OF THE MEDICINAL PRODUCTS, ROUTE OF ADMINISTRATION AND MARKETING AUTHORISATION HOLDERS IN THE MEMBER STATES

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Austria	Novartis Pharma GmbH Stella-Klein-Löw-Weg 17 A-1020 Wien (Tel: + 43-1-8665 70)	Diovan 40 mg Filmtabletten	40 mg	film-coated tablets	Oral Use
Austria	Novartis Pharma GmbH Stella-Klein-Löw-Weg 17 A-1020 Wien (Tel: + 43-1-8665 70)	Angiosan 40 mg Filmtabletten	40 mg	film-coated tablets	Oral Use
Austria	Novartis Pharma GmbH Stella-Klein-Löw-Weg 17 A-1020 Wien (Tel: + 43-1-8665 70)	Diovan 80 mg Filmtabletten	80 mg	film-coated tablets	Oral Use
Austria	Novartis Pharma GmbH Stella-Klein-Löw-Weg 17 A-1020 Wien (Tel: + 43-1-8665 70)	Angiosan 80 mg Filmtabletten	80 mg	film-coated tablets	Oral Use
Austria	Novartis Pharma GmbH Stella-Klein-Löw-Weg 17 A-1020 Wien (Tel: + 43-1-8665 70)	Diovan 160 mg Filmtabletten	160 mg	film-coated tablets	Oral Use
Austria	Novartis Pharma GmbH Stella-Klein-Löw-Weg 17 A-1020 Wien (Tel: + 43-1-8665 70)	Angiosan 160 mg Filmtabletten	160 mg	film-coated tablets	Oral Use
Austria	Novartis Pharma GmbH Stella-Klein-Löw-Weg 17 A-1020 Wien (Tel: + 43-1-8665 70)	Diovan 320 mg Filmtabletten	320 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Austria	Novartis Pharma GmbH Stella-Klein-Löw-Weg 17 A-1020 Wien (Tel: + 43-1-8665 70)	Angiosan 320 mg Filmtabletten	320 mg	film-coated tablets	Oral Use
Belgium	N.V. Novartis Pharma S.A. Medialaan 40, bus 1 B-1800 Vilvoorde (Tel: +32-2-246 16 11)	Diovane 40 mg	40 mg	film-coated tablets	Oral Use
Belgium	N.V. Novartis Pharma S.A. Medialaan 40, bus 1 B-1800 Vilvoorde (Tel: +32-2-246 16 11)	Diovane 80 mg	80 mg	film-coated tablets	Oral Use
Belgium	N.V. Novartis Pharma S.A. Medialaan 40, bus 1 B-1800 Vilvoorde (Tel: +32-2-246 16 11)	Diovane 160 mg	160 mg	film-coated tablets	Oral Use
Belgium	N.V. Novartis Pharma S.A. Medialaan 40, bus 1 B-1800 Vilvoorde (Tel: +32-2-246 16 11)	Diovane 320 mg	320 mg	film-coated tablets	Oral Use
Bulgaria	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Bulgaria	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Bulgaria	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Bulgaria	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
Cyprus	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Cyprus	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Cyprus	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Cyprus	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
Czech Republic	NOVARTIS s.r.o. Pharma Nagano III. U Nákladového nádraží 10 130 00 Praha 3 (Tel +420-2-2577 51 11)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Czech Republic	NOVARTIS s.r.o. Pharma Nagano III. U Nákladového nádraží 10 130 00 Praha 3 (Tel +420-2-2577 51 11)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Denmark	Novartis Healthcare A/S Lyngbyvej 172 DK-2100 København Ø (Tel: +45-39-16 84 00)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Denmark	Novartis Healthcare A/S Lyngbyvej 172 DK-2100 København Ø (Tel: +45-39-16 84 00)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Denmark	Novartis Healthcare A/S Lyngbyvej 172 DK-2100 København Ø (Tel: +45-39-16 84 00)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Denmark	Novartis Healthcare A/S Lyngbyvej 172 DK-2100 København Ø (Tel: +45-39-16 84 00)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Estonia	Novartis Finland OY Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan	40 mg	film-coated tablets	Oral Use
Estonia	Novartis Finland OY Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan	80 mg	film-coated tablets	Oral Use
Estonia	Novartis Finland OY Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan	160 mg	film-coated tablets	Oral Use
Estonia	Novartis Finland OY Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan	320 mg	film-coated tablets	Oral Use
Finland	Novartis Finland Oy Metsänneidonkuja 10 FIN-02130 Espoo (Tel: + 358-9-6133 22 11)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Finland	Novartis Finland Oy Metsänneidonkuja 10 FIN-02130 Espoo (Tel: + 358-9-6133 22 11)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Finland	Novartis Finland Oy Metsänneidonkuja 10 FIN-02130 Espoo (Tel: + 358-9-6133 22 11)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Finland	Novartis Finland Oy Metsänneidonkuja 10 FIN-02130 Espoo (Tel: + 358-9-6133 22 11)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
France	Novartis Pharma S.A.S. 2 and 4, rue Lionel Terray 92500 RUEIL-MALMAISON (Tel: +33-1-5547 60 00)	Tareg 40 mg	40 mg	film-coated tablets	Oral Use
France	Novartis Pharma S.A.S. 2 and 4, rue Lionel Terray 92500 RUEIL-MALMAISON (Tel: +33-1-5547 60 00)	Tareg 80 mg	80 mg	film-coated tablets	Oral Use
France	Novartis Pharma S.A.S. 2 and 4, rue Lionel Terray 92500 RUEIL-MALMAISON (Tel: +33-1-5547 60 00)	Tareg 160 mg	160 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Cordinate 40 mg	40 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Provas 40 mg	40 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Cordinate 80 mg	80 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Provas 80 mg	80 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Diovan 160 mg protect	160 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Cordinate 160 mg	160 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Provas 160 mg	160 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Diovan 320 mg forte	320 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Cordinate 320 mg	320 mg	film-coated tablets	Oral Use
Germany	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg (Tel: +49-911-273-0)	Provas 320 mg	320 mg	film-coated tablets	Oral Use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
Greece	Novartis (Hellas) S.A.C.I. National Road No. 1 (12th Km) Metamorphosis GR-144 51 Athens (Tel: +30-210-281 17 12)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Greece	Novartis (Hellas) S.A.C.I. National Road No. 1 (12th Km) Metamorphosis GR-144 51 Athens (Tel: +30-210-281 17 12)	Dalzad 40 mg	40 mg	film-coated tablets	Oral Use
Greece	Novartis (Hellas) S.A.C.I. National Road No. 1 (12th Km) Metamorphosis GR-144 51 Athens (Tel: +30-210-281 17 12)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Greece	Novartis (Hellas) S.A.C.I. National Road No. 1 (12th Km) Metamorphosis GR-144 51 Athens (Tel: +30-210-281 17 12)	Dalzad 80 mg	80 mg	film-coated tablets	Oral Use
Greece	Novartis (Hellas) S.A.C.I. National Road No. 1 (12th Km) Metamorphosis GR-144 51 Athens (Tel: +30-210-281 17 12)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Greece	Novartis (Hellas) S.A.C.I. National Road No. 1 (12th Km) Metamorphosis GR-144 51 Athens (Tel: +30-210-281 17 12)	Dalzad 160 mg	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Greece	Novartis (Hellas) S.A.C.I. National Road No. 1 (12th Km) Metamorphosis GR-144 51 Athens (Tel: +30-210-281 17 12)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
Greece	Novartis (Hellas) S.A.C.I. National Road No. 1 (12th Km) Metamorphosis GR-144 51 Athens (Tel: +30-210-281 17 12)	Dalzad 320 mg	320 mg	film-coated tablets	Oral Use
Hungary	Novartis Hungaria Kft. Bartók Béla út 43-47 H-1114 Budapest (Tel: +36-1-457 65 00)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Hungary	Novartis Hungaria Kft. Bartók Béla út 43-47 H-1114 Budapest (Tel: +36-1-457 65 00)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Hungary	Novartis Hungaria Kft. Bartók Béla út 43-47 H-1114 Budapest (Tel: +36-1-457 65 00)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Hungary	Novartis Hungaria Kft. Bartók Béla út 43-47 H-1114 Budapest (Tel: +36-1-457 65 00)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
Iceland	Novartis Healthcare A/S Lyngbyvej 172 DK-2100 København Ø Denmark (Tel: +45-39-16 84 00)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Iceland	Novartis Healthcare A/S Lyngbyvej 172 DK-2100 København Ø Denmark (Tel: +45-39-16 84 00)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Iceland	Novartis Healthcare A/S Lyngbyvej 172 DK-2100 København Ø Denmark (Tel: +45-39-16 84 00)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Iceland	Novartis Healthcare A/S Lyngbyvej 172 DK-2100 København Ø Denmark (Tel: +45-39-16 84 00)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
Ireland	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Ireland	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Ireland	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Ireland	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
Italy	Novartis Farma S.p.A. Largo Umberto Boccioni 1 I-21040 Origgio (Tel: + 39-02-96542214)	Tareg 40 mg	40 mg	film-coated tablets	Oral Use
Italy	Novartis Farma S.p.A. Largo Umberto Boccioni 1 I-21040 Origgio (Tel: + 39-02-96542214)	Rixil 40 mg	40 mg	film-coated tablets	Oral Use
Italy	Novartis Farma S.p.A. Largo Umberto Boccioni 1 I-21040 Origgio (Tel: + 39-02-96542214)	Tareg 80 mg	80 mg	film-coated tablets	Oral Use
Italy	Novartis Farma S.p.A. Largo Umberto Boccioni 1 I-21040 Origgio (Tel: + 39-02-96542214)	Rixil 80 mg	80 mg	film-coated tablets	Oral Use
Italy	Novartis Farma S.p.A. Largo Umberto Boccioni 1 I-21040 Origgio (Tel: + 39-02-96542214)	Tareg 160 mg	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Italy	Novartis Farma S.p.A. Largo Umberto Boccioni 1 I-21040 Origgio (Tel: + 39-02-96542214)	Rixil 160 mg	160 mg	film-coated tablets	Oral Use
Italy	Novartis Farma S.p.A. Largo Umberto Boccioni 1 I-21040 Origgio (Tel: + 39-02-96542214)	Tareg 320 mg	320 mg	film-coated tablets	Oral Use
Italy	Novartis Farma S.p.A. Largo Umberto Boccioni 1 I-21040 Origgio (Tel: + 39-02-96542214)	Rixil 320 mg	320 mg	film-coated tablets	Oral Use
Latvia	Novartis Finland OY Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Latvia	Novartis Finland OY Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Latvia	Novartis Finland OY Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Latvia	Novartis Finland OY Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Lithuania	Novartis Finland Oy Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan 80 mg plėvele dengtos tabletės	80 mg	film-coated tablets	Oral Use
Lithuania	Novartis Finland Oy Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan 160 mg plėvele dengtos tabletės	160 mg	film-coated tablets	Oral Use
Lithuania	Novartis Finland Oy Metsänneidonkuja 10 FIN-02130 Espoo Finland (Tel: + 358-9-6133 22 11)	Diovan 320 mg plėvele dengtos tabletės	320 mg	film-coated tablets	Oral Use
Luxembourg	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Luxembourg	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Luxembourg	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Luxembourg	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
Malta	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Malta	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Malta	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Malta	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR United Kingdom (Tel: +44-1276-69 22 55)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Netherlands	Novartis Pharma B.V. Postbus 241 NL-6824 DP Arnhem (Tel: + 31-26-378 21 00)	Diovan 40	40 mg	film-coated tablets	Oral Use
Netherlands	Novartis Pharma B.V. Postbus 241 NL-6800 LZ Arnhem (Tel: + 31-26-378 21 00)	Diovan 80	80 mg	film-coated tablets	Oral Use
Netherlands	Novartis Pharma B.V. Postbus 241 NL-6824 DP Arnhem (Tel: + 31-26-378 21 00)	Diovan 160	160 mg	film-coated tablets	Oral Use
Netherlands	Novartis Pharma B.V. Postbus 241 NL-6824 DP Arnhem (Tel: + 31-26-378 21 00)	Diovan 320	320 mg	film-coated tablets	Oral Use
Norway	Novartis Norge AS Brynsalléen 4 Postboks 237 Økern NO-0510 Oslo (Tel: +47-2305 20 00)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Norway	Novartis Norge AS Brynsalléen 4 Postboks 237 Økern NO-0510 Oslo (Tel: +47-2305 20 00)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Norway	Novartis Norge AS Brynsalléen 4 Postboks 237 Økern NO-0510 Oslo (Tel: +47-2305 20 00)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Norway	Novartis Norge AS Brynsalléen 4 Postboks 237 Økern NO-0510 Oslo (Tel: +47-2305 20 00)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
Poland	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan	40 mg	film-coated tablets	Oral Use
Poland	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan	80 mg	film-coated tablets	Oral Use
Poland	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan	160 mg	film-coated tablets	Oral Use
Poland	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan	320 mg	film-coated tablets	Oral Use
Portugal	Novartis Farma - Produtos Farmacêuticos S.A. Rua do Centro Empresarial, Edificio 8 Quinta da Beloura P-2710-444 Sintra (Tel: +351 21 000 86 00)	Diovan	40 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Portugal	Laboratório Normal-Produtos Farmacêuticos, Lda Rua do Centro Empresarial, Edificio 8 Quinta da Beloura P-2710-444 Sintra (Tel: +351 21 000 86 00)	Tareg	40 mg	film-coated tablets	Oral Use
Portugal	Novartis Farma - Produtos Farmacêuticos S.A. Rua do Centro Empresarial, Edificio 8 Quinta da Beloura P-2710-444 Sintra (Tel: +351 21 000 86 00)	Diovan	80 mg	film-coated tablets	Oral Use
Portugal	Laboratório Normal-Produtos Farmacêuticos, Lda Rua do Centro Empresarial, Edificio 8 Quinta da Beloura P-2710-444 Sintra (Tel: +351 21 000 86 00)	Tareg	80 mg	film-coated tablets	Oral Use
Portugal	Novartis Farma - Produtos Farmacêuticos S.A. Rua do Centro Empresarial, Edificio 8 Quinta da Beloura P-2710-444 Sintra (Tel: +351 21 000 86 00)	Diovan	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Portugal	Laboratório Normal-Produtos Farmacêuticos, Lda Rua do Centro Empresarial, Edificio 8 Quinta da Beloura P-2710-444 Sintra (Tel: +351 21 000 86 00)	Tareg	160 mg	film-coated tablets	Oral Use
Portugal	Novartis Farma - Produtos Farmacêuticos S.A. Rua do Centro Empresarial, Edificio 8 Quinta da Beloura P-2710-444 Sintra (Tel: +351 21 000 86 00)	Diovan	320 mg	film-coated tablets	Oral Use
Romania	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 40 mg, film coated tablets	40 mg	film-coated tablets	Oral Use
Romania	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 80 mg, film coated tablets	80 mg	film-coated tablets	Oral Use
Romania	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 160 mg, film coated tablets	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Slovak Republic	NOVARTIS s.r.o. Pharma Nagano III. U Nákladového nádraží 10 130 00 Praha 3 Czech Republic (Tel +420-2-2577 51 11)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
Slovak Republic	NOVARTIS s.r.o. Pharma Nagano III. U Nákladového nádraží 10 130 00 Praha 3 Czech Republic (Tel +420-2-2577 51 11)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
Slovak Republic	NOVARTIS s.r.o. Pharma Nagano III. U Nákladového nádraží 10 130 00 Praha 3 Czech Republic (Tel +420-2-2577 51 11)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use
Slovak Republic	NOVARTIS s.r.o. Pharma Nagano III. U Nákladového nádraží 10 130 00 Praha 3 Czech Republic (Tel +420-2-2577 51 11)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use
Slovenia	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 40 mg filmsko obložene tablete	40 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Slovenia	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 80 mg filmsko obložene tablete	80 mg	film-coated tablets	Oral Use
Slovenia	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 160 mg filmsko obložene tablete	160 mg	film-coated tablets	Oral Use
Slovenia	Novartis Pharma GmbH Roonstrasse 25 D-90429 Nürnberg Germany (Tel: +49-911-273-0)	Diovan 320 mg filmsko obložene tablete	320 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Diován Cardio 40 mg comprimidos recubiertos con película	40 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Kalpress Cardio 40 mg comprimidos recubiertos con película	40 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Miten Cardio 40 mg comprimidos recubiertos con película	40 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Diován 80 mg comprimidos recubiertos con película	80 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Kalpress 80 mg comprimidos recubiertos con película	80 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Miten 80 mg comprimidos recubiertos con película	80 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Diován 160 mg comprimidos recubiertos con película	160 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Kalpress 160 mg comprimidos recubiertos con película	160 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Miten 160 mg comprimidos recubiertos con película	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Diován 320 mg comprimidos recubiertos con película	320 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Kalpress 320 mg comprimidos recubiertos con película	320 mg	film-coated tablets	Oral Use
Spain	Novartis Farmacéutica, S.A. Gran Via de les Corts Catalanes, 764 08013 Barcelona (Tel: +34-93-306 42 00)	Miten 320 mg comprimidos recubiertos con película	320 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Diovan	40 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Angiosan	40 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Valsartan Novartis	40 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Diovan	80 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Angiosan	80 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Valsartan Novartis	80 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Diovan	160 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Angiosan	160 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Valsartan Novartis	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical Form	Route of administration
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Diovan	320 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Angiosan	320 mg	film-coated tablets	Oral Use
Sweden	Novartis Sverige AB Kemistvägen 1B P.O. Box 1150 SE-183 11 Täby (Tel: + 46-8-732 32 00)	Valsartan Novartis	320 mg	film-coated tablets	Oral Use
United Kingdom	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR (Tel: +44-1276-69 22 55)	Diovan 40 mg	40 mg	film-coated tablets	Oral Use
United Kingdom	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR (Tel: +44-1276-69 22 55)	Diovan 80 mg	80 mg	film-coated tablets	Oral Use
United Kingdom	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR (Tel: +44-1276-69 22 55)	Diovan 160 mg	160 mg	film-coated tablets	Oral Use

Member State EU/EEA	**Marketing Authorisation Holder**	**Invented name**	**Strength**	**Pharmaceutical Form**	**Route of administration**
United Kingdom	Novartis Pharmaceuticals UK Ltd Frimley Business Park Frimley, Camberley Surrey GU16 7SR (Tel: +44-1276-69 22 55)	Diovan 320 mg	320 mg	film-coated tablets	Oral Use

ANNEX II

AMENDMENTS TO SUMMARY OF PRODUCT CHARACTERISTICS AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Diovan and associated names 3 mg/ml oral solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml solution contains 3 mg of valsartan.

Excipients:
Each ml solution contains 0.3 g sucrose, 1.62 mg methyl parahydroxybenzoate (E218) and 5 mg poloxamer (188)

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Clear, colourless to pale yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of hypertension in children and adolescents 6 to 18 years of age.

4.2 Posology and method of administration

Posology
Children and adolescents 6 to 18 years of age
For children who are unable to swallow tablets, the use of the Diovan oral solution up to 80 mg valsartan (corresponding to 27 ml) is recommended. The systemic exposure and peak plasma concentration of valsartan is higher with the solution compared to the tablets.

The initial dose for the Diovan oral solution is 20 mg (corresponding to 7 ml of the solution) once daily for children below 35 kg of weight and 40 mg (corresponding to 13 ml of the solution) once daily for those weighing 35 kg or more. The dose should be adjusted based on blood pressure response up to a maximum dose of 80 mg valsartan (corresponding to 27 ml of the solution).

It is not recommended to switch between Diovan tablets and Diovan oral solution unless clinically required as there is insufficient information to guide an appropriate dose on switching between the two formulations. Indirect comparisons suggest that, the oral bioavailability of valsartan with the solution is approximately 2-fold higher than the tablets.
Therefore, if switching from Diovan tablets to Diovan oral solution is considered essential on clinical grounds, the valsartan dose should be adjusted as described in the table below and blood pressure should be carefully monitored. The dose should be titrated based on blood pressure response and tolerability.

Tablets	Solution	
Valsartan dose	Valsartan dose to provide when switching	Volume to take
40 mg	20 mg	7 ml
80 mg	40 mg	13 ml
160 mg	80 mg	27 ml
320 mg	Due to the high volume of solution that would be necessary, the use of the solution is not recommended	Not applicable

If switching from Diovan oral solution to Diovan tablets is considered clinically essential, initially the same dose in milligrams should be given. Subsequently, frequent blood pressure monitoring should be performed taking into account potential under-dosing and dose should be titrated further based on blood pressure response and tolerability.

Children less than 6 years of age
Available data are described in sections 4.8, 5.1 and 5.2. However safety and efficacy of Diovan in children aged 1 to 6 years have not been established.

Use in paediatric patients aged 6 to 18 years with renal impairment
Use in paediatric patients with a creatinine clearance <30 ml/min and paediatric patients undergoing dialysis has not been studied, therefore valsartan is not recommended in these patients. No dose adjustment is required for paediatric patients with a creatinine clearance >30 ml/min. Renal function and serum potassium should be closely monitored (see sections 4.4 and 5.2).

Use in paediatric patients aged 6 to 18 years with hepatic impairment
As in adults, Diovan is contraindicated in paediatric patients with severe hepatic impairment, biliary cirrhosis and in patients with cholestasis (see sections 4.3, 4.4 and 5.2). There is limited clinical experience with Diovan in paediatric patients with mild to moderate hepatic impairment. The dose of valsartan should not exceed 80 mg in these patients.

Paediatric heart failure and recent myocardial infarction
Diovan is not recommended for the treatment of heart failure or recent myocardial infarction in children and adolescents below the age of 18 years due to the lack of data on safety and efficacy.

Method of administration
Diovan may be taken independently of a meal.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients.
- Severe hepatic impairment, biliary cirrhosis and cholestasis.
- Second and third trimester of pregnancy (see sections 4.4 and 4.6).

4.4 Special warnings and precautions for use

Hyperkalaemia
Concomitant use with potassium supplements, potassium-sparing diuretics, salt substitutes containing potassium, or other agents that may increase potassium levels (heparin, etc.) is not recommended. Monitoring of potassium should be undertaken as appropriate.

Impaired renal function
There is currently no experience on the safe use in patients with a creatinine clearance <10 ml/min and patients undergoing dialysis, therefore valsartan should be used with caution in these patients. No dose adjustment is required for adult patients with creatinine clearance >10 ml/min (see sections 4.2 and 5.2).

Hepatic impairment
In patients with mild to moderate hepatic impairment without cholestasis, Diovan should be used with caution (see sections 4.2 and 5.2).

Sodium- and/or volume-depleted patients
In severely sodium-depleted and/or volume-depleted patients, such as those receiving high doses of diuretics, symptomatic hypotension may occur in rare cases after initiation of therapy with Diovan. Sodium and/or volume depletion should be corrected before starting treatment with Diovan, for example by reducing the diuretic dose.

Renal artery stenosis
In patients with bilateral renal artery stenosis or stenosis to a solitary kidney, the safe use of Diovan has not been established.
Short-term administration of Diovan to twelve patients with renovascular hypertension secondary to unilateral renal artery stenosis did not induce any significant changes in renal haemodynamics, serum creatinine, or blood urea nitrogen (BUN). However, other agents that affect the renin-angiotensin system may increase blood urea and serum creatinine in patients with unilateral renal artery stenosis, therefore monitoring of renal function is recommended when patients are treated with valsartan.

Kidney transplantation
There is currently no experience on the safe use of Diovan in patients who have recently undergone kidney transplantation.

Primary hyperaldosteronism
Patients with primary hyperaldosteronism should not be treated with Diovan as their renin-angiotensin system is not activated.

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

Diabetes
Diovan oral solution contains 0,3 g sucrose per mililiter. This should be taken into account in patients with diabetes mellitus.

Hereditary fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency
Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take Diovan oral solution as it contains sucrose.

Methyl parahydroxybenzoate
Diovan oral solution contains methyl parahydroxybenzoate which may cause allergic reactions (possibly delayed).

Diovan oral solution contains poloxamer (188) which may cause softened stools.

Pregnancy
Angiotensin II Receptor Antagonists (AIIRAs) should not be initiated during pregnancy. Unless continued AIIRAs therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive 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).

Other conditions with stimulation of the renin-angiotensin system
In patients whose renal function may depend on the activity of the renin-angiotensin system (e.g patients with severe congestive heart failure), treatment with angiotensin converting enzyme

inhibitors has been associated with oliguria and/or progressive azotaemia and in rare cases with acute renal failure and/or death. As valsartan is an angiotensin II antagonist, it cannot be excluded that the use of Diovan may be associated with impairment of the renal function.

Paediatric population

Change of pharmaceutical form
Diovan oral solution is not bioequivalent to the tablet formulation and patients should not be switched unless clinically essential. For dosing recommendations in this case, see section 4.2.

Impaired renal function
Use in paediatric patients with a creatinine clearance <30 ml/min and paediatric patients undergoing dialysis has not been studied, therefore valsartan is not recommended in these patients. No dose adjustment is required for paediatric patients with a creatinine clearance >30 ml/min (see sections 4.2 and 5.2). Renal function and serum potassium should be closely monitored during treatment with valsartan. This applies particularly when valsartan is given in the presence of other conditions (fever, dehydration) likely to impair renal function.

Impaired hepatic function
As in adults, Diovan is contraindicated in paediatric patients with severe hepatic impairment, biliary cirrhosis and in patients with cholestasis (see sections 4.3 and 5.2). There is limited clinical experience with Diovan in paediatric patients with mild to moderate hepatic impairment. The dose of valsartan should not exceed 80 mg in these patients.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant use not recommended

Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concurrent use of ACE inhibitors. Due to the lack of experience with concomitant use of valsartan and lithium, this combination is not recommended. If the combination proves necessary, careful monitoring of serum lithium levels is recommended.

Potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium and other substances that may increase potassium levels
If a medicinal product that affects potassium levels is considered necessary in combination with valsartan, monitoring of potassium plasma levels is advised.

Caution required with concomitant use

Non-steroidal anti-inflammatory medicines (NSAIDs), including selective COX-2 inhibitors, acetylsalicylic acid >3 g/day), and non-selective NSAIDs
When angiotensin II antagonists are administered simultaneously with NSAIDs, attenuation of the antihypertensive effect may occur. Furthermore, concomitant use of angiotensin II antagonists and NSAIDs may lead to an increased risk of worsening of renal function and an increase in serum potassium. Therefore, monitoring of renal function at the beginning of the treatment is recommended, as well as adequate hydration of the patient.

Others
In drug interaction studies with valsartan, no interactions of clinical significance have been found with valsartan or any of the following substances: cimetidine, warfarin, furosemide, digoxin, atenolol, indometacin, hydrochlorothiazide, amlodipine, glibenclamide.

Paediatric population
In hypertension in children and adolescents, where underlying renal abnormalities are common, caution is recommended with the concomitant use of valsartan and other substances that inhibit the renin angiotensin aldosterone system which may increase serum potassium. Renal function and serum potassium should be closely monitored.

4.6 Fertility, pregnancy and lactation

Pregnancy

The use of Angiotensin II Receptor Antagonists (AIIRAs) is not recommended during the first trimester of pregnancy (see section 4.4). The use of AIIRAs is contra-indicated during the second and third trimester 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 anti-hypertensive 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. AIIRAs therapy exposure 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, hyperkalemia); see also section 5.3 “Preclinical safety data”. 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 also sections 4.3 and 4.4).

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

Fertility
Valsartan had no adverse effects on the reproductive performance of male or female rats at oral doses up to 200 mg/kg/day. This dose is 6 times the maximum recommended human dose on a mg/m^2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient).

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive have been performed. When driving vehicles or operating machines it should be taken into account that occasionally dizziness or weariness may occur.

4.8 Undesirable effects

In controlled clinical studies in adult patients with hypertension, the overall incidence of adverse reactions (ADRs) was comparable with placebo and is consistent with the pharmacology of valsartan. The incidence of ADRs did not appear to be related to dose or treatment duration and also showed no association with gender, age or race.

The ADRs reported from clinical studies, post-marketing experience and laboratory findings are listed below according to system organ class.

Adverse reactions are ranked by frequency, the most frequent first, using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000) very rare (<1/10,000), including isolated reports. Within each frequency grouping, adverse reactions are ranked in order of decreasing seriousness.
For all the ADRs reported from post-marketing experience and laboratory findings, it is not possible to apply any ADR frequency and therefore they are mentioned with a "not known" frequency.

- Hypertension

Blood and lymphatic system disorders	
Not known	Decrease in haemoglobin, Decrease in haematocrit, Neutropenia, Thrombocytopenia
Immune system disorders	
Not known	Hypersensitivity including serum sickness
Metabolism and nutrition disorders	
Not known	Increase of serum potassium
Ear and labyrinth system disorders	
Uncommon	Vertigo
Vascular disorders	
Not known	Vasculitis
Respiratory, thoracic and mediastinal disorders	
Uncommon	Cough
Gastrointestinal disorders	
Uncommon	Abdominal pain
Hepato-biliary disorders	
Not known	Elevation of liver function values including increase of serum bilirubin
Skin and subcutaneous tissue disorders	
Not known	Angioedema, Rash, Pruritus
Musculoskeletal and connective tissue disorders	
Not known	Myalgia
Renal and urinary disorders	
Not known	Renal failure and impairment, Elevation of serum creatinine
General disorders and administration site conditions	
Uncommon	Fatigue

Paediatric population

Hypertension
The antihypertensive effect of valsartan has been evaluated in two randomised, double-blind clinical studies in 561 paediatric patients from 6 to 18 years of age. With the exception of isolated gastrointestinal disorders (like abdominal pain, nausea, vomiting) and dizziness, no relevant differences in terms of type, frequency and severity of adverse reactions were identified between the safety profile for paediatric patients aged 6 to 18 years and that previously reported for adult patients.

Neurocognitive and developmental assessment of paediatric patients aged 6 to 16 years of age revealed no overall clinically relevant adverse impact after treatment with Diovan for up to one year.

In a double-blind randomized study in 90 children aged 1 to 6 years, which was followed by a one-year open-label extension, two deaths and isolated cases of marked liver transaminases elevations were observed. These cases occurred in a population who had significant comorbidities. A causal relationship to Diovan has not been established. In a second study in which 75 children aged 1 to

6 years were randomised, no significant liver transaminase elevations or death occurred with valsartan treatment.

Hyperkalaemia was more frequently observed in children and adolescents aged 6 to 18 years with underlying chronic kidney disease.

The safety profile seen in controlled-clinical studies in adult patients with post-myocardial infarction and/or heart failure varies from the overall safety profile seen in hypertensive patients. This may relate to the patients underlying disease. ADRs that occurred in adult patients with post-myocardial infarction and/or heart failure are listed below.

- Post-myocardial infarction and/or heart failure (studied in adult patients only)

Blood and lymphatic system disorders	
Not known	Thrombocytopenia
Immune system disorders	
Not known	Hypersensitivity including serum sickness
Metabolism and nutrition disorders	
Uncommon	Hyperkalaemia
Not known	Increase of serum potassium
Nervous system disorders	
Common	Dizziness, Postural dizziness
Uncommon	Syncope, Headache
Ear and labyrinth system disorders	
Uncommon	Vertigo
Cardiac disorders	
Uncommon	Cardiac failure
Vascular disorders	
Common	Hypotension, Orthostatic hypotension
Not known	Vasculitis
Respiratory, thoracic and mediastinal disorders	
Uncommon	Cough
Gastrointestinal disorders	
Uncommon	Nausea, Diarrhoea
Hepato-biliary disorders	
Not known	Elevation of liver function values
Skin and subcutaneous tissue disorders	
Uncommon	Angioedema
Not known	Rash, Pruritis
Musculoskeletal and connective tissue disorders	
Not known	Myalgia
Renal and urinary disorders	
Common	Renal failure and impairment
Uncommon	Acute renal failure, Elevation of serum creatinine
Not known	Increase in Blood Urea Nitrogen
General disorders and administration site conditions	
Uncommon	Asthenia, Fatigue

4.9 Overdose

Symptoms
Overdose with Diovan may result in marked hypotension, which could lead to depressed level of consciousness, circulatory collapse and/or shock.

Treatment
The therapeutic measures depend on the time of ingestion and the type and severity of the symptoms; stabilisation of the circulatory condition is of prime importance.
If hypotension occurs, the patient should be placed in a supine position and blood volume correction should be undertaken.
Valsartan is unlikely to be removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Angiotensin II Antagonists, plain, ATC code: C09CA03

Valsartan is an orally active, potent, and specific angiotensin II (Ang II) receptor antagonist. It acts selectively on the AT_1 receptor subtype, which is responsible for the known actions of angiotensin II. The increased plasma levels of Ang II following AT_1 receptor blockade with valsartan may stimulate the unblocked AT_2 receptor, which appears to counterbalance the effect of the AT_1 receptor.
Valsartan does not exhibit any partial agonist activity at the AT_1 receptor and has much (about 20,000 fold) greater affinity for the AT_1 receptor than for the AT_2 receptor. Valsartan is not known to bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.
Valsartan does not inhibit ACE (also known as kininase II) which converts Ang I to Ang II and degrades bradykinin. Since there is no effect on ACE and no potentiation of bradykinin or substance P, angiotensin II antagonists are unlikely to be associated with coughing. In clinical trials where valsartan was compared with an ACE inhibitor, the incidence of dry cough was significantly ($p<0.05$) less in patients treated with valsartan than in those treated with an ACE inhibitor (2.6% versus 7.9% respectively). In a clinical trial of patients with a history of dry cough during ACE inhibitor therapy, 19.5% of trial subjects receiving valsartan and 19.0% of those receiving a thiazide diuretic experienced cough compared to 68.5% of those treated with an ACE inhibitor ($p<0.05$).

Use in adults
Administration of Diovan to patients with hypertension results in reduction of blood pressure without affecting pulse rate.
In most patients, after administration of a single oral dose, onset of antihypertensive activity occurs within 2 hours, and the peak reduction of blood pressure is achieved within 4-6 hours. The antihypertensive effect persists over 24 hours after dosing. During repeated dosing, the antihypertensive effect is substantially present within 2 weeks, and maximal effects are attained within 4 weeks and persist during long-term therapy. Combined with hydrochlorothiazide, a significant additional reduction in blood pressure is achieved.
Abrupt withdrawal of Diovan has not been associated with rebound hypertension or other adverse clinical events.
In hypertensive patients with type 2 diabetes and microalbuminuria, valsartan has been shown to reduce the urinary excretion of albumin. The MARVAL (Micro Albuminuria Reduction with Valsartan) study assessed the reduction in urinary albumin excretion (UAE) with valsartan (80-160 mg/od) versus amlodipine (5-10 mg/od), in 332 type 2 diabetic patients (mean age: 58 years; 265 men) with microalbuminuria (valsartan: 58 µg/min; amlodipine: 55.4 µg/min), normal or high blood pressure and with preserved renal function (blood creatinine <120 µmol/l). At 24 weeks, UAE was reduced ($p<0.001$) by 42% (–24.2 µg/min; 95% CI: –40.4 to –19.1) with valsartan and approximately 3% (–1.7 µg/min; 95% CI: –5.6 to 14.9) with amlodipine despite similar rates of blood pressure reduction in both groups.
The Diovan Reduction of Proteinuria (DROP) study further examined the efficacy of valsartan in reducing UAE in 391 hypertensive patients (BP=150/88 mmHg) with type 2 diabetes, albuminuria (mean=102 µg/min; 20-700 µg/min) and preserved renal function (mean serum creatinine = 80 µmol/l). Patients were randomized to one of 3 doses of valsartan (160, 320 and 640 mg/od) and treated for 30 weeks. The purpose of the study was to determine the optimal dose of valsartan for

reducing UAE in hypertensive patients with type 2 diabetes. At 30 weeks, the percentage change in UAE was significantly reduced by 36% from baseline with valsartan 160 mg (95%CI: 22 to 47%), and by 44% with valsartan 320 mg (95%CI: 31 to 54%). It was concluded that 160-320 mg of valsartan produced clinically relevant reductions in UAE in hypertensive patients with type 2 diabetes.

Hypertension (paediatric population)
The antihypertensive effect of valsartan have been evaluated in four randomized, double-blind clinical studies in 561 paediatric patients from 6 to 18 years of age and 165 paediatric patients 1 to 6 years of age. Renal and urinary disorders, and obesity were the most common underlying medical conditions potentially contributing to hypertension in the children enrolled in these studies.

Clinical experience in children at or above 6 years of age
In a clinical study involving 261 hypertensive paediatric patients 6 to 16 years of age, patients who weighed <35 kg received 10, 40 or 80 mg of valsartan tablets daily (low, medium and high doses), and patients who weighed ≥35 kg received 20, 80, and 160 mg of valsartan tablets daily (low, medium and high doses). At the end of 2 weeks, valsartan reduced both systolic and diastolic blood pressure in a dose-dependent manner. Overall, the three dose levels of valsartan (low, medium and high) significantly reduced systolic blood pressure by 8, 10, 12 mmHg from the baseline, respectively. Patients were re-randomized to either continue receiving the same dose of valsartan or were switched to placebo. In patients who continued to receive the medium and high doses of valsartan, systolic blood pressure at trough was -4 and -7 mm Hg lower than patients who received the placebo treatment. In patients receiving the low dose of valsartan, systolic blood pressure at trough was similar to that of patients who received the placebo treatment. Overall, the dose-dependent antihypertensive effect of valsartan was consistent across all the demographic subgroups.

In another clinical study involving 300 hypertensive paediatric patients 6 to 18 years of age, eligible patients were randomized to receive valsartan or enalapril tablets for 12 weeks. Children weighing between ≥18 kg and <35 kg received valsartan 80 mg or enalapril 10 mg; those between ≥35 kg and <80 kg received valsartan 160 mg or enalapril 20 mg; those ≥80 kg received valsartan 320 mg or enalapril 40 mg. Reductions in systolic blood pressure were comparable in patients receiving valsartan (15 mmHg) and enalapril (14 mm Hg) (non-inferiority p-value <0.0001). Consistent results were observed for diastolic blood pressure with reductions of 9.1 mmHg and 8.5 mmHg with valsartan and enalapril, respectively.

Clinical experience in children less than 6 years of age
Two clinical studies were conducted in patients aged 1 to 6 years with 90 and 75 patients, respectively. No children below the age of 1 year were enrolled in these studies. In the first study, the efficacy of valsartan was confirmed compared to placebo but a dose-response could not be demonstrated. In the second study, higher doses of valsartan were associated with greater BP reductions, but the dose response trend did not achieve statistical significance and the treatment difference compared to placebo was not significant. Because of these inconsistencies, valsartan is not recommended in this age group (see section 4.8).

The European Medicines Agency has waived the obligation to submit the results of studies with Diovan in all subsets of the paediatric population in heart failure and heart failure after recent myocardial infarction. See section 4.2 for information on paediatric use.

5.2 Pharmacokinetic properties

Absorption:
Following oral administration of valsartan alone, peak plasma concentrations of valsartan are reached in 2–4 hours with tablets and 1–2 hours with solution formulation. Mean absolute bioavailability is 23% and 39% with tablets and solution formulation, respectively. Food decreases exposure (as measured by AUC) to valsartan by about 40% and peak plasma concentration (C_{max}) by about 50%, although from about 8 h post dosing plasma valsartan concentrations are similar for the fed and fasted

groups. This reduction in AUC is not, however, accompanied by a clinically significant reduction in the therapeutic effect, and valsartan can therefore be given either with or without food.

Distribution:
The steady-state volume of distribution of valsartan after intravenous administration is about 17 litres, indicating that valsartan does not distribute into tissues extensively. Valsartan is highly bound to serum proteins (94–97%), mainly serum albumin.

Biotransformation:
Valsartan is not biotransformed to a high extent as only about 20% of dose is recovered as metabolites. A hydroxy metabolite has been identified in plasma at low concentrations (less than 10% of the valsartan AUC). This metabolite is pharmacologically inactive.

Excretion:
Valsartan shows multiexponential decay kinetics ($t_{½\alpha}$ <1 h and $t_{½\beta}$ about 9 h). Valsartan is primarily eliminated by biliary excretion in faeces (about 83% of dose) and renally in urine (about 13% of dose), mainly as unchanged drug. Following intravenous administration, plasma clearance of valsartan is about 2 l/h and its renal clearance is 0.62 l/h (about 30% of total clearance). The half-life of valsartan is 6 hours.

Special populations

Impaired renal function
As expected for a compound where renal clearance accounts for only 30% of total plasma clearance, no correlation was seen between renal function and systemic exposure to valsartan. Dose adjustment is therefore not required in patients with renal impairment (creatinine clearance >10 ml/min). There is currently no experience on the safe use in patients with a creatinine clearance <10 ml/min and patients undergoing dialysis, therefore valsartan should be used with caution in these patients (see sections 4.2 and 4.4).
Valsartan is highly bound to plasma protein and is unlikely to be removed by dialysis.

Hepatic impairment
Approximately 70% of the dose absorbed is eliminated in the bile, essentially in the unchanged form. Valsartan does not undergo any noteworthy biotransformation. A doubling of exposure (AUC) was observed in patients with mild to moderate hepatic impairment compared to healthy subjects. However, no correlation was observed between plasma valsartan concentration versus degree of hepatic dysfunction. Diovan has not been studied in patients with severe hepatic dysfunction (see sections 4.2, 4.3 and 4.4).

Paediatric population
In a study of 26 paediatric hypertensive patients (aged 1 to 16 years) given a single dose of a suspension of valsartan (mean: 0.9 to 2 mg/kg, with a maximum dose of 80 mg), the clearance (litres/h/kg) of valsartan was comparable across the age range of 1 to 16 years and similar to that of adults receiving the same formulation.

Impaired renal function
Use in paediatric patients with a creatinine clearance <30 ml/min and paediatric patients undergoing dialysis has not been studied, therefore valsartan is not recommended in these patients. No dose adjustment is required for paediatric patients with a creatinine clearance >30 ml/min. Renal function and serum potassium should be closely monitored (see sections 4.2 and 4.4).

5.3 Preclinical safety data

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

In rats, maternally toxic doses (600 mg/kg/day) during the last days of gestation and lactation led to lower survival, lower weight gain and delayed development (pinna detachment and ear-canal opening) in the offspring (see section 4.6). These doses in rats (600 mg/kg/day) are approximately 18 times the maximum recommended human dose on a mg/m^2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient).
In non-clinical safety studies, high doses of valsartan (200 to 600 mg/kg body weight) caused in rats a reduction of red blood cell parameters (erythrocytes, haemoglobin, haematocrit) and evidence of changes in renal haemodynamics (slightly raised plasma urea, and renal tubular hyperplasia and basophilia in males). These doses in rats (200 and 600 mg/kg/day) are approximately 6 and 18 times the maximum recommended human dose on a mg/m^2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient).
In marmosets at similar doses, the changes were similar though more severe, particularly in the kidney where the changes developed to a nephropathy which included raised urea and creatinine. Hypertrophy of the renal juxtaglomerular cells was also seen in both species. All changes were considered to be caused by the pharmacological action of valsartan which produces prolonged hypotension, particularly in marmosets. For therapeutic doses of valsartan in humans, the hypertrophy of the renal juxtaglomerular cells does not seem to have any relevance.

Paediatric population
Daily oral dosing of neonatal/juvenile rats (from a postnatal day 7 to postnatal day 70) with valsartan at doses as low as 1 mg/kg/day (about 10-35% of the maximum recommended paediatric dose of 4 mg/kg/day on systemic exposure basis)produced persistent, irreversible kidney damage. These effects above mentioned represent an expected exaggerated pharmacological effect of angiotensin converting enzyme inhibitors and angiotensin II type 1 blockers; such effects are observed if rats are treated during the first 13 days of life. This period coincides with 36 weeks of gestation in humans, which could occasionally extend up to 44 weeks after conception in humans. The rats in the juvenile valsartan study were dosed up to day 70, and effects on renal maturation (postnatal 4-6 weeks) cannot be excluded. Functional renal maturation is an ongoing process within the first year of life in humans. Consequently, a clinical relevance in children <1 year of age cannot be excluded, while preclinical data do not indicate a safety concern for children older than 1 year.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Methyl parahydroxybenzoate (E218)
Potassium sorbate
Poloxamer (188)
Citric acid, anhydrous
Sodium citrate
Artificial blueberry flavour (538926 C)
Propylene glycol (E1520)
Sodium hydroxide
Hydrochloric acid
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

18 months

6.4 Special precautions for storage

Do not store above 30°C.
Once opened, the bottle can be stored for up to 3 months at temperatures below 30°C.

6.5 Nature and contents of container

180 ml amber type III glass bottle with a white child resistant polypropylene cap, including a polyethylene sealing disk and a yellow tamper evident ring, in addition the pack includes one dispensing kit containing one 5 ml oral dosing polypropylene syringe, one press in bottle adapter and one 30 ml polypropylene dosing cup.
Pack size: 1 bottle containing 160 ml oral solution

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

8. MARKETING AUTHORISATION NUMBER

[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]

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTON/BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT

Diovan and associated names 3 mg/ml oral solution
Valsartan

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each ml contains 3 mg of valsartan.

3. LIST OF EXCIPIENTS

Contains sucrose, methyl parahydroxybenzoate (E218) and poloxamer (188) (see leaflet for further information).

4. PHARMACEUTICAL FORM AND CONTENTS

1 bottle containing 160 ml oral solution.
1 dispenser kit containing one press in bottle adapter, one 5 ml oral syringe and one 30 ml dosing cup.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE 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

Do not store above 30°C. Once opened, the bottle can be stored for up to 3 months below 30°C.

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

[To be completed nationally]

16. INFORMATION IN BRAILLE

[To be completed nationally]

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Diovan and associated names 3 mg/ml oral solution
Valsartan

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 DIOVAN IS AND WHAT IT IS USED FOR

Diovan belongs to a class of medicines known as angiotensin II receptor antagonists, which help to control high blood pressure. Angiotensin II is a substance in the body that causes vessels to tighten, thus causing your blood pressure to increase. Diovan works by blocking the effect of angiotensin II. As a result, blood vessels relax and blood pressure is lowered.

Diovan 3 mg/ml oral solution **can be used to treat high blood pressure in children and adolescents 6 to 18 years of age.** High blood pressure increases the workload on the heart and arteries. If not treated it can damage the blood vessels of the brain, heart, and kidneys, and may result in a stroke, heart failure, or kidney failure. High blood pressure increases the risk of heart attacks. Lowering your blood pressure to normal reduces the risk of developing these disorders.

2. BEFORE YOU TAKE DIOVAN

Do not take Diovan:
- if you are **allergic** (hypersensitive) to valsartan or any of the other ingredients of Diovan listed at the end of this leaflet.
- if you have **severe liver disease.**
- if you are **more than 3 months pregnant** (it is also better to avoid Diovan in early pregnancy - see pregnancy section).

If any of these apply to you, do not take Diovan

Take special care with Diovan:
- if you have liver disease.
- if you have severe kidney disease or if you are undergoing dialysis**.**
- if you are suffering from a narrowing of the kidney artery.
- if you have recently undergone kidney transplantation (received a new kidney).
- if you have severe heart disease, your doctor may check your kidney function.
- if you are taking medicines that increase the amount of potassium in your blood. These include potassium supplements or salt substitutes containing potassium, potassium-sparing medicines

and heparin. It may be necessary to check the amount of potassium in your blood at regular intervals.
- if you are below 18 years of age and you take Diovan in combination with other medicines that inhibit the renin angiotensin aldosterone system (medicines that lower blood pressure), your doctor may check your kidney function and the amount of potassium in your blood at regular intervals.
- if you suffer from aldosteronism. This is a disease in which your adrenal glands make too much of the hormone aldosterone. If this applies to you, the use of Diovan is not recommended.
- if you have lost a lot of fluid (dehydration) caused by diarrhoea, vomiting, or high doses of water tablets (diuretics).
- you must tell your doctor if you think you are (or might become) pregnant. Diovan 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).

If any of these apply to you, tell your doctor before you take Diovan.

Taking other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

The effect of the treatment can be influenced if Diovan is taken together with certain other medicines. It may be necessary to change the dose, to take other precautions, or in some cases to stop taking one of the medicines. This applies to both prescription and non-prescription medicines, especially:
- **other medicines that lower blood pressure**, especially **water tablets** (diuretics).
- **medicines that increase the amount of potassium** in your blood. These include potassium supplements or salt substitutes containing potassium, potassium-sparing medicines and heparin.
- **certain type of pain killers** called non-steroidal anti-inflammatory medicines **(NSAIDs)**.
- **lithium**, a medicine used to treat some types of psychiatric illness.

Taking Diovan with food and drink
You can take Diovan with or without food.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.

- **You must tell your doctor if you think that you are (or might become) pregnant**. Your doctor will normally advise you to stop taking Diovan before you become pregnant or as soon as you know you are pregnant, and will advise you to take another medicine instead of Diovan. Diovan 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 it is used after the third month of pregnancy.

- **Tell your doctor if you are breast-feeding or about to start breast-feeding.** Diovan 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
Before you drive a vehicle, use tools or operate machines, or carry out other activities that require concentration, make sure you know how Diovan affects you. Like many other medicines used to treat high blood pressure, Diovan may in rare cases cause dizziness and affect the ability to concentrate.

Important information about some of the ingredients of Diovan solution
- Diovan solution contains 0.3 g **sucrose** per millilitre. Take this into account if you have diabetes mellitus. If you have been told by your doctor that you have an intolerance to some

sugars, contact your doctor before taking Diovan solution. The amount of sucrose in the Diovan solution may be harmful to your teeth.
- Diovan solution contains **methyl parahydroxybenzoate** (E218). This may cause allergic reactions possibly occuring some time after you take the solution. The signs may include rash, itching, hives. If any of the side effects gets serious. please tell your doctor.
- Diovan solution contains **poloxamer (188)**. This may soften your stools.

3. HOW TO TAKE DIOVAN

Always take Diovan exactly as your doctor has told you in order to get the best results and reduce the risk of side effects. You should check with your doctor or pharmacist if you are not sure. People with high blood pressure often do not notice any signs of this problem. Many may feel quite normal. This makes it all the more important for you to keep your appointments with the doctor even if you are feeling well.

Please read the instructions at the end of this leaflet before you use the oral syringe or the dosing cup.

How much to take
Take Diovan solution once a day
- If you weigh less than 35 kg
    - the usual dose is 20 mg of valsartan (corresponding to 7 ml of the solution).
- If you weigh 35 kg or more:
    - the usual dose is 40 mg of valsartan (corresponding to 13 ml of the solution).

In some cases your doctor may ask you to take up to 80 mg of valsartan (corresponding to 27 ml of the solution).

You can take Diovan with or without food.
Take Diovan at about the same time each day.

If you take more Diovan than you should
If you experience severe dizziness and/or fainting, contact your doctor immediately and lie down. If you have accidentally taken more Diovan solution than you should, contact your doctor, pharmacist, or hospital.

If you forget to take Diovan
If you forget to take a dose, take it as soon as you remember. However, if it is almost time for your next dose, skip the dose you missed.

Do not take a double dose to make up for a forgotten dose.

If you stop taking Diovan
Stopping your treatment with Diovan may cause your disease to get worse. Do not stop taking your medicine unless your doctor tells you to.

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

4. POSSIBLE SIDE EFFECTS

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

These side effects may occur with certain frequencies, which are defined as follows:
- very common: affects more than 1 user in 10

- common: affects 1 to 10 users in 100
- uncommon: affects 1 to 10 users in 1,000
- rare: affects 1 to 10 users in 10,000
- very rare: affects less than 1 user in 10,000
- not known: frequency cannot be estimated from the available data.

Some symptoms need immediate medical attention:
You may experience symptoms of angioedema (a specific allergic reaction), such as
- swollen face, lips, tongue or throat
- difficulty in breathing or swallowing
- hives, itching

If you get any of these, see a doctor immediately.

Side effects include:

Common
- dizziness
- low blood pressure with or without symptoms such as dizziness and fainting when standing up
- decreased kidney function (signs of renal impairment)

Uncommon
- angioedema (see section "Some symptoms need immediate medical attention")
- sudden loss of consciousness (syncope)
- spinning sensation (vertigo)
- severely decreased kidney function (signs of acute renal failure)
- muscle spasms, abnormal heart rhythm (signs of hyperkalaemia)
- breathlessness, difficulty breathing when lying down, swelling of the feet or legs (signs of cardiac failure)
- headache
- cough
- abdominal pain
- nausea
- diarrhoea
- tiredness
- weakness

Not known
- allergic reactions with rash, itching and hives; symptoms of fever, swollen joints and joint pain, muscle pain, swollen lymph nodes and/or flu-like symptoms may occur (signs of serum sickness)
- purplish-red spots, fever, itching (signs of inflammation of blood vessels also called vasculitis)
- unusual bleeding or bruising (signs of thrombocytopenia)
- muscle pain (myalgia)
- fever, sore throat or mouth ulcers due to infections (symptoms of low level of white blood cells also called neutropenia)
- decrease of level of haemoglobin and decrease of the percentage of red blood cells in the blood (which can lead to anaemia in severe cases)
- increase of level of potassium in the blood (which can trigger muscle spasms and abnormal heart rhythm in severe cases)
- elevation of liver function values (which can indicate liver damage) including an increase of bilirubin in the blood (which can trigger yellow skin and eyes in severe cases)
- increase of level of blood urea nitrogen and increase of level of serum creatinine (which can indicate abnormal kidney function)

The frequency of some side effects may vary depending on your condition. For example, side effects such as dizziness, and decreased kidney function, were seen less frequently in adult patients treated with high blood pressure than in adult patients treated for heart failure or after a recent heart attack.

Side effects in children and adolescents are similar to those seen in adults.

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.

5. HOW TO STORE DIOVAN

- Do not store above 30°C.
- Once opened, the bottle can be stored for up to 3 months at temperatures below 30°C.
- Keep out of the reach and sight of children.
- Do not use Diovan after the expiry date which is stated on the pack. The expiry date refers to the last day of that month.
- Do not use Diovan if you notice that the pack is damaged or shows signs of tampering.
- 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 Diovan contains
- The active substance is valsartan.
- 1 ml oral solution contains 3 mg of valsartan.
- The other ingredients are sucrose, methyl parahydroxybenzoate (E218), potassium sorbate, poloxamer (188), citric acid anhydrous, sodium citrate, artificial blueberry flavour, propylene glycol (E1520), sodium hydroxide, hydrochloric acid, purified water.

What Diovan looks like and contents of the pack
Diovan 3 mg/ml oral solution is a clear, colourless to pale yellow solution.
- The solution is supplied in a pack containing one 180 ml amber glass bottle with a child-resistant screw cap and a yellow tamper evident ring. The bottle contains 160 ml of solution. It comes with a dispensing kit containing one press in bottle adapter, one 5 ml oral polypropylene dosing syringe and one 30 ml polypropylene dosing cup.

Marketing Authorisation Holder and Manufacturer

[To be completed nationally]

For any information about this medicine, please contact the Marketing Authorisation Holder.

This leaflet was last approved in

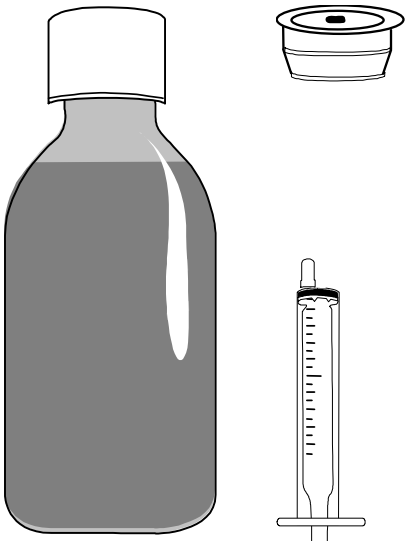
This medicinal product is authorised in the Member States of the EEA under the following names:

[To be completed nationally]

INSTRUCTIONS FOR USING THE ORAL SYRINGE AND THE DOSING CUP

Please read these instructions carefully before taking the medicine. This will help you to use the oral syringe and the dosing cup correctly.

What you will be using



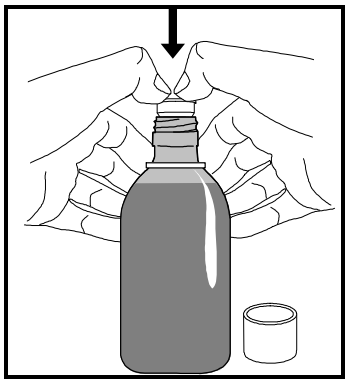
A press in bottle adapter:
- that you insert into the neck of the bottle.
- Once you have inserted it, do not remove it.

A bottle containing the medicine:
- that has a child- resistant screw cap.
- Always screw the cap back on after use.

An oral dosing syringe:
- that consists of a clear plastic tube with a plunger inside.
- The oral syringe fits into the bottle adapter and is used to measure out the required amount of medicine from the bottle. Use a new bottle adapter and oral dosing syringe each time you start a new bottle of medicine.

A dosing cup:
- that can be used if the prescribed dose requires filling the syringe several times.
- Always put the dosing cup back onto the cap after use and cleaning.

Fitting the press in bottle adapter into a new bottle of medicine

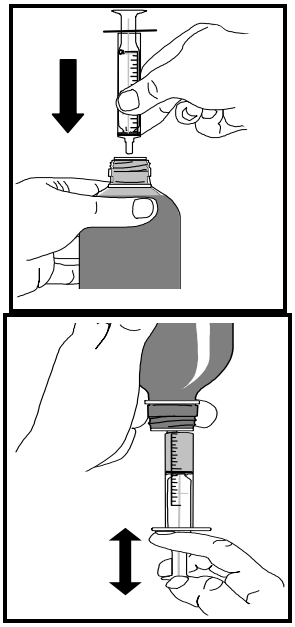


1. Remove the cap from the bottle by pushing it down **firmly** and turning it anti-clockwise (as shown on the top of the cap).
2. Holding the open bottle upright on a table, push the bottle adapter **firmly** into the neck of the bottle as far as it will go.

Note: You may not be able to push the bottle adapter down fully but this does not matter as it will be forced into the bottle when you screw the cap back on.

3. Screw the cap back on the bottle.

Preparing a dose of medicine



4. Remove the cap from the bottle by pushing it down **firmly** and turning it anti-clockwise (as shown on the top of the cap).

5. Check that the plunger is pushed fully into the oral syringe.

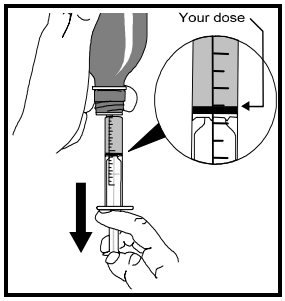
6. Keeping the bottle upright, insert the oral syringe **firmly** into the bottle adapter.

7. Holding the oral syringe in place, carefully turn the bottle and oral syringe upside down.

8. Before you measure your dose you need to get rid of any large bubbles that may be trapped in the oral syringe. To do this:
   - slowly pull the plunger all the way out so that the oral syringe fills with medicine.
   - then, push the plunger all the way back in so that it is empty again.

Measuring a dose of medicine

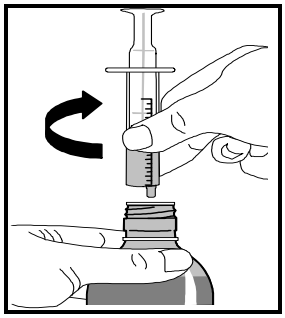
Note: The total amount of solution that can be measured into the oral syringe is 5 ml. Depending on the prescribed dose, it may be necessary to repeat steps 10 to 16 several times. For example, if the prescribed dose is 13 ml, it will be necessary to measure out the solution in three separate stages: 5 ml + 5 ml + 3 ml.



9. Find the marker on the oral syringe that corresponds to the required amount of medicine.

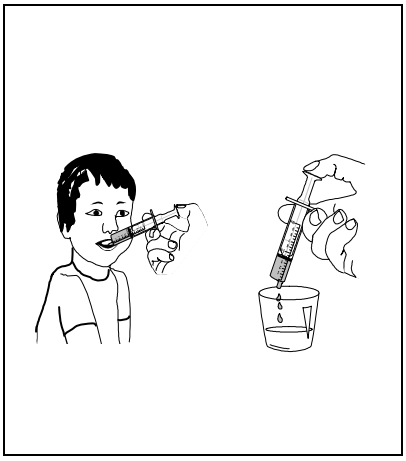
10. Slowly pull the plunger out until the top edge of the black ring inside is exactly level with the marker.

11. Carefully turn the bottle and oral syringe back upright.



12. Remove the oral syringe from the bottle adapter by gently twisting it out.

Taking the medicine



13. Sit upright.

14. Put the end of the oral syringe into the mouth.

15. Slowly push the plunger in and swallow the medicine directly from the oral syringe.

16. If the prescribed dose requires filling the syringe several times, **you can empty the measured doses of medicine from the syringe into the dosing cup** and then check the total volume of solution.

17. Drink the entire solution right away.
18. Replace the child-resistant screw cap after use.

19. **To clean the oral syringe:**
    - Wipe the outside of the oral syringe with a clean, dry tissue.
    - Do this after each time that you use the oral syringe.

20. **To clean the cup:**
    - Rinse the cup with clean water.
    - Dry the cup with a clean tissue and place it back over the cap of the bottle.

ANNEX III

CONDITIONS OF THE MARKETING AUTHORISATION

The National Health Authorities 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 Diovan at National level, taking into account the new paediatric data and the CHMP recommendations. The Risk Management Plan should include the following:
  - In the safety specification:
    - results of juvenile safety studies regarding the risk of nephrotoxicity and its relevance for the use in the different paediatric groups
    - paediatric exposure in clinical trials and in post marketing use by age group, indication (including off label use), dose, duration of use, gender and ethnicity
  - As safety concerns:
    - Identified risks: hyperkalemia and hypotension.
    - Potential risks: renal impairment, elevation of liver function values, hypersensitivity including angioedema and serum sickness, hemoglobin/hematocrit decreased and medication error including overdose.
    - Missing information: clinical management and use of pharmacotherapy in paediatric heart failure, paediatric recent myocardial infarction, paediatric hypertension with renal impairment (GFR < 30 mL/min) and paediatric hypertension with mild to moderate hepatic impairment.
    - Use in children under 6 years of age.
    - Need for dose adaptation when switching between oral solution and tablets.
  - In the pharmacovigilance plan:
    - Targeted checklists for follow up of adverse events listed above as potential risks in the paediatric population
    - A study primarily aimed at establishing the long-term safety in CKD and non-CKD paediatric patients. The protocol of the study will be submitted by the applicant in the second quarter of 2010 for agreement with the CHMP with input from the PDCO. The study report will be finalized by the first quarter of 2014.
    - A physician survey of clinical management and uses of medicinal products in pediatric patients with heart failure. The final study report should be submitted by the last quarter of 2010.
    - A long term study in the younger age group (1 to 5 years old). The applicant will initiate a scientific dialogue via the CHMP's Scientific Advice with the involvement of the PDCO for protocol assistance with the aim of gaining further insight on a hypertensive clinical trial in younger children with valsartan and to define objectives and design parameters in investigating the efficacy in this population. When a viable and mutually agreed study plan emerges from the dialogue, a new study will be initiated within one year.
    - A comparative bioavailability study confirming the relative dosing of the tablets and oral solution should be carried out. The study report will be finalized by Q4 2010.

- Restart the cycle of PSUR submission for Diovan as follows:
  - Six-monthly PSURs until two full years of experience with the paediatric indication in the EU has been gained
  - Yearly PSURs for the following two years
  - Thereafter submission at 3-yearly intervals

  The PSURs should focus on the use in the paediatric population.