ANNEX 1

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

Member State	Marketing Authorisation Holder	Invented name	Strength	Pharmaceutical form	Route of administration
Austria	Gerot Pharmazeutika GesmbH Arnethgasse 3 A-1160 Wien Austria	Allenopar 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	Allen Pharmazeutika GesmbH Albert Schweitzer Gasse 6 A-1140 Wien Austria	Paroxetin 'Allen' 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	Arcana Arzneimittel GmbH Zimbagasse 5 A-1147 Wien Austria	Paroxetin 'Arcana' 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	Sandoz GmbH Biochemiestrasse 10 A-6250 Kundl/Tirol Austria	Paluxetil 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	GlaxoSmithKline Pharma GmbH Albert Schweitzer Gasse 6 A-1140 Wien Austria	Seroxat 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	GlaxoSmithKline Pharma GmbH Albert Schweitzer Gasse 6 A-1140 Wien Austria	Seroxat 2 mg / ml – oral suspension	2 mg / ml	Oral suspension	Oral use
Austria	GlaxoSmithKline Pharma GmbH Albert Schweitzer Gasse 6 A-1140 Wien Austria	Glaxopar 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use

Austria	GlaxoSmithKline Pharma GmbH Albert Schweitzer Gasse 6 A-1140 Wien Austria	Paroglax 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	GlaxoSmithKline Pharma GmbH Albert Schweitzer Gasse 6 A-1140 Wien Austria	Paroxetin 'GSK' 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	Hexal Pharma GmbH Wilhelminestrasse 91/IIf/3 A-1160 Wien Austria	Paroxat 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	Hexal Pharma GmbH Wilhelminestrasse 91/IIf/3 A-1160 Wien Austria	Paroxat 40 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	Interpharm Produktions GmbH Effingergasse 21 A-1160 Wien Austria	Paroxetin 'Interpharm' Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	Lannacher Heilmittel GmbH Schlossplatz 1 A-8502 Lannach Austria	Ennos 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	Ratiopharm Arzneimittel Vertriebs – GmbH Albert Schweitzer Gasse 3 A-1140 Wien Austria	Paroxetin 'Merckle' 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use

Austria	Ratiopharm Arzneimittel Vertriebs – GmbH Albert Schweitzer Gasse 3 A-1140 Wien Austria	Paroxetin 'ratiopharm' 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Austria	Stada Arzneimittel GmbH Heiligenstädter str. 52 A-1190 Wien Austria	Parocetan 20 mg – Filmtabletten	20 mg	Film-coated tablet	Oral use
Belgium	Bexal Av J. Bordet 168, 1140 Brussels, Belgium	Paroxetine Bexal 20 mg	20 mg	Film-coated tablet	Oral use
Belgium	Bexal Av J. Bordet 168, 1140 Brussels, Belgium	Paroxetine Bexal 40 mg	40 mg	Film-coated tablet	Oral use
Belgium	Eurogenerics N.V. Heizel Esplanade Heysel B 22 B-1020 Brussel Belgium	Paroxetine EG 20 mg	20 mg	Film-coated tablet	Oral use
Belgium	GlaxoSmithKline s.a./n.v. Rue du Tilleul 13 B-1332 Genval Belgium	Aropax	20 mg	Tablet	Oral use
Belgium	GlaxoSmithKline s.a./n.v. Rue du Tilleul 13 B-1332 Genval Belgium	Aropax	30 mg	Tablet	Oral use
Belgium	GlaxoSmithKline s.a./n.v. Rue du Tilleul 13 B-1332 Genval Belgium	Aropax Suspension orale	2 mg / ml	Oral suspension	Oral use

Belgium	GlaxoSmithKline s.a./n.v. Rue du Tilleul 13 B-1332 Genval Belgium	Seroxat	20 mg	Tablet	Oral use
Belgium	GlaxoSmithKline s.a./n.v. Rue du Tilleul 13 B-1332 Genval Belgium	Seroxat	30 mg	Tablet	Oral use
Belgium	GlaxoSmithKline s.a./n.v. Rue du Tilleul 13 B-1332 Genval Belgium	Seroxat Suspension orale	2 mg / ml	Oral suspension	Oral use
Belgium	Medis-Danmark A/S Havelse Molle 14 DK-3600 Frederikssund Danmark	Parocetan 20 mg	20 mg	Film-coated tablet	Oral use
Belgium	Medis-Danmark A/S Havelse Molle 14 DK-3600 Frederikssund Danmark	Paroxetiphar 20 mg	20 mg	Film-coated tablet	Oral use
Belgium	Ratiopharm Belgium s.a./n.v. Rue Aaint-Lambert 141 B-1200 Bruxelles Belgium	Paroxetine – Ratiopharm 20 mg	20 mg	Film-coated tablet	Oral use
Belgium	Merck n.v./s.a. Brusselsesteennweg 288 B-3090 Overijse Belgium	Merck – Paroxetine 20 mg	20 mg	Film-coated tablet	Oral use
Cyprus	Medochemie Ltd, 1-10 Constantinoupoleos str. P.O. Box 51407 3505 Lemesos Cyprus	Arketis	20 mg	Film-coated tablet	Oral use

Cyprus	Medochemie Ltd, 1-10 Constantinoupoleos str. P.O. Box 51407 3505 Lemesos Cyprus	Arketis	30 mg	Film-coated tablet	Oral use
Cyprus	SmithKline Beecham PLC 980, Great West Road Brentford Middlesex UK	Seroxat	20 mg	Tablet	Oral use
Cyprus	SmithKline Beecham PLC 980, Great West Road Brentford Middlesex UK	Seroxat	30 mg	Tablet	Oral use
Czech Republic	Apotex Europe Ltd Rowan House 41 London Street, Reading, Berkshire, RG1 4PS, UK	Apo-Parox	20 mg	Film-coated tablet	Oral use
Czech Republic	Hexal A/S, Kanalholmen 8-12, 2650 Hvidovre, Denmark	Parolex 20	20 mg,	Film-coated tablet	Oral use
Czech Republic	Hexal A/S, Kanalholmen 8-12, 2650 Hvidovre, Denmark	Parolex 40	40 mg	Film-coated tablet	Oral use
Czech Republic	Ratiopharm GmbH, Graf-Arco-Strasse 3, D-890 79 Ulm, Germany	Paroxetin-Ratiopharm 20 mg	20 mg	Film-coated tablet	Oral use

Czech Republic	Chemical works of Gedeon Richter Ltd, Gyömröi út 19-21, 1103 Budapest, Hungary	Remood 20 mg	20 mg	Film-coated tablet	Oral use
Czech Republic	Chemical works of Gedeon Richter Ltd, Gyömröi út 19-21, 1103 Budapest, Hungary	Remood 30 mg	30 mg	Film-coated tablet	Oral use
Czech Republic	Smithkline Beecham Pharmaceuticals New Horizont Court, TW8 9EP Brentford, Middlesex UK	Seroxat 20 mg	20 mg	Film-coated tablet	Oral use
Czech Republic	Smithkline Beecham Pharmaceuticals New Horizont Court, TW8 9EP Brentford, Middlesex UK	Seroxat 30 mg	30 mg	Film-coated tablet	Oral use
Denmark	1A Farma A/S Herstedøstervej 27-29 2620 Albertslund Denmark	Paroxetine '1A Farma'	20 mg	Film-coated tablet	Oral use
Denmark	1A Farma A/S Herstedøstervej 27-29 2620 Albertslund Denmark	Paroxetine '1A Farma'	40 mg	Film-coated tablet	Oral use

Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Oxetine	20 mg	Film-coated tablet	Oral use
Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroxetin 'GEA'	20 mg	Film-coated tablet	Oral use
Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroxetin 'GEA'	40 mg	Film-coated tablet	Oral use
Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroc	20 mg	Film-coated tablet	Oral use
Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroc	40 mg	Film-coated tablet	Oral use
Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroneurin	20 mg	Film-coated tablet	Oral use
Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroneurin	40 mg	Film-coated tablet	Oral use
Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Optipar	20 mg	Film-coated tablet	Oral use

Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Optipar	40 mg	Film-coated tablet	Oral use
Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Roxac	20 mg	Film-coated tablet	Oral use
Denmark	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Roxac	40 mg	Film-coated tablet	Oral use
Denmark	Alpharma AS Harbitzalléen 3 Skøyen, 0212 Oslo Norge	Paroxetin 'Alpharma'	20 mg	Film-coated tablet	Oral use
Denmark	Sandoz GmbH Biochemiestrasse 10 A-6250 Kundl Austria	Paroxetin 'Biochemie'	20 mg	Film-coated tablet	Oral use
Denmark	Sandoz GmbH Biochemiestrasse 10 A-6250 Kundl Austria	Paroxetin 'Biochemie'	30 mg	Film-coated tablet	Oral use
Denmark	DuraScan Medical Products A/S Svendborgvej 243 5260 Odense S Denmark	Serodur	20 mg	Film-coated tablet	Oral use
Denmark	Generics (UK) Limited Station Close Potters Bar Hertfordshire EN6 1TL UK	Paroxetin 'Generics'	20 mg	Film-coated tablet	Oral use

Denmark	Generics (UK) Limited Station Close Potters Bar Hertfordshire EN6 1TL UK	Pasero	20 mg	Film-coated tablet	Oral use
Denmark	Genthon BV Microweg 22 6545 CM Nijmegen The Netherlands	Paroxetin 'Genthon'	20 mg	Film-coated tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykær 68 DK-2605 Brøndby Denmark	Seroxat	20 mg	Film-coated tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykær 68 DK-2605 Brøndby Denmark	Seroxat	30 mg	Film-coated tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykær 68 DK-2605 Brøndby Denmark	Seroxat	2 mg / ml	Oral suspension	Oral use
Denmark	NM Pharma A/S Lautrupvang 8 DK-2750 Ballerup Denmark	Paroxetin 'NM'	20 mg	Film-coated tablet	Oral use
Denmark	NM Pharma A/S Lautrupvang 8 DK-2750 Ballerup Denmark	Paroxetin 'NM'	30 mg	Film-coated tablet	Oral use

Denmark	PharmaCoDane Aps Marielundvej 46 A 2730 Herlev Denmark	Paroxetin 'PCD'	20 mg	Film-coated tablet	Oral use
Denmark	Copyfarm A/S Energivej 15 5260 Odense S Denmark	Paroxetin 'Copyfarm	20 mg	Film-coated tablet	Oral use
Denmark	Copyfarm A/S Energivej 15 5260 Odense S Denmark	Paroxetine 'Copyfarm'	30 mg	Film-coated tablet	Oral use
Denmark	Pharmascope Ltd. Unit 107 Ashbourne Industrial Estate Co. Meath Ireland	Meparox	20 mg	Film-coated tablet	Oral use
Denmark	Pharmascope Ltd. Unit 107 Ashbourne Industrial Estate Co. Meath Ireland	Meparox	30 mg	Film-coated tablet	Oral use
Denmark	Pharmascope Ltd. Unit 107 Ashbourne Industrial Estate Co. Meath Ireland	Paroscope	20 mg	Film-coated tablet	Oral use
Denmark	Pharmascope Ltd. Unit 107 Ashbourne Industrial Estate Co. Meath Ireland	Paroscope	30 mg	Film-coated tablet	Oral use

Denmark	United Nordic Pharma A/S Hammervej 7 2970 Hørsholm Denmark	Paroxetin 'UNP'	20 mg	Film-coated tablet	Oral use
Denmark	United Nordic Pharma A/S Hammervej 7 2970 Hørsholm Denmark	Paroxetin 'UNP'	30 mg	Film-coated tablet	Oral use
Denmark	Ratiopharm GmbH Graf-Arco-Strasse 3 D-89079 Ulm Germany	Paroxegen	20 mg	Film-coated tablet	Oral use
Denmark	Ratiopharm GmbH Graf-Arco-Strasse 3 D-89079 Ulm Germany	Paroxegen	30 mg	Film-coated tablet	Oral use
Denmark	Ratiopharm GmbH Graf-Arco-Strasse 3 D-89079 Ulm Germany	Paroxetin 'Ratiopharm'	20 mg	Film-coated tablet	Oral use
Denmark	Ratiopharm GmbH Graf-Arco-Strasse 3 D-89079 Ulm Germany	Sopax	20 mg	Film-coated tablet	Oral use
Denmark	Ratiopharm GmbH Graf-Arco-Strasse 3 D-89079 Ulm Germany	Pasorex	20 mg	Film-coated tablet	Oral use
Denmark	Scand Pharm Generics AB Ynglingagatan 14, 5tr S-11347 Stockholm Sweden	Serorex	20 mg	Film-coated tablet	Oral use

Denmark	Scand Pharm Generics AB Ynglingagatan 14, 5tr S-11347 Stockholm Sweden	Serorex	30 mg	Film-coated tablet	Oral use
Denmark	Scand Pharm Generics AB Ynglingagatan 14, 5tr S-11347 Stockholm Sweden	Seroxetabs	20 mg	Film-coated tablet	Oral use
Denmark	Synthon BV Microweg 22 6545 CM Nijmegen The Netherlands	Euplix	20 mg	Film-coated tablet	Oral use
Denmark	Synthon BV Microweg 22 6545 CM Nijmegen The Netherlands	Paroxetin 'Synthon'	20 mg	Film-coated tablet	Oral use
Denmark	Synthon BV Microweg 22 6545 CM Nijmegen The Netherlands	Parsyn	20 mg	Film-coated tablet	Oral use
Denmark	Synthon BV Microweg 22 6545 CM Nijmegen The Netherlands	Varoxetin	20 mg	Film-coated tablet	Oral use
Estonia	Glaxo Group Ltd Berkeley Avenue, Greenford Middlesex TW8 9GS United Kingdom	Paroxat	20 mg	Film-coated tablet	Oral use
Estonia	Hexal AG Industriestrasse 25 83607 Holzkirchen Germany	Paroxetinhexal 20	20 mg	Tablet	Oral use

Estonia	Hexal AG Industriestrasse 25 83607 Holzkirchen Germany	Paroxetinhexal 40	40 mg	Tablet	Oral use
Estonia	Richter Gyömröi ut 19-21 H-1103 Budapest X Hungary	Rexetin	20 mg	Tablet	Oral use
Estonia	Richter Gyömröi ut 19-21 H-1103 Budapest X Hungary	Rexetin 30 mg	30 mg	Tablet	Oral use
Estonia	SmithKline Beecham 980 Great West Road, Brentford Middlesex TW8 9GS United Kingdom	Seroxat	20 mg	Tablet	Oral use
Estonia	SmithKline Beecham 980 Great West Road, Brentford Middlesex TW8 9GS United Kingdom	Seroxat	30 mg	Coated tablet	Oral use
Finland	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Optipar	20 mg	Film-coated tablet	Oral use
Finland	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Optipar	40 mg	Film-coated tablet	Oral use
Finland	Genthon BV Microweg 22 6545 CM NIJMEGEN The Netherlands	Euplix	20 mg	Film-coated tablet	Oral use

Finland	Pharmcom Oy Keijumaki 6B 30 02130 Espoo Finland	Parox	20 mg	Film-coated tablet	Oral use
Finland	Ratiopharm GmbH Graf-Arco-Strasse 3 D-89079 Ulm Germany	Paroxetin ratiopharm	20 mg	Film-coated tablet	Oral use
Finland	SmithKline Beecham Plc 980 Great West Road Brentford Middlesex TW8 9GS UK	Seroxat	20 mg	Film-coated tablet	Oral use
Finland	SmithKline Beecham Plc 980 Great West Road Brentford Middlesex TW8 9GS UK	Seroxat	2 mg / ml	Oral suspension	Oral use
Finland	STADA Arzneimittel AG Stadastrasse 2-18 61118 BAD VILBEL Germany	Paroxetin Stada	20 mg	Film-coated tablet	Oral use
France	Chiesi SA 11 Avenue Dubonnet 92400 Courbevoie France	Divarius	20 mg	Coated tablet	Oral use
France	Laboratoires G GAM Europarc 33 rue Auguste Perret 94042 creteil cedex France	Paroxetine G GAM	20 mg	Coated tablet	Oral use

France	Laboratoires G GAM Europarc 33 rue Auguste Perret 94042 creteil cedex France	Paroxetine G GAM	40 mg	Coated tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 route de Versailles 78163 Marly-le-Roy France	Deroxat	20 mg	Coated tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 route de Versailles 78163 Marly-le-Roy France	Deroxat	20 mg / 10 ml	Oral suspension	Oral use
France	Laboratoire GlaxoSmithKline 100 route de Versailles 78163 Marly-le-Roy France	Paroxetine GSK	20 mg	Coated tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 route de Versailles 78163 Marly-le-Roy France	Paroxetine GSK	20 mg / 10 ml	Oral suspension	Oral use
France	Laboratoire Paucourt 100 route de Versailles 78163 Marly-le-Roy France	Paroxetine Paucourt	20 mg / 10 ml	Oral suspension	Oral use
France	KIRON Pharmaceutica BV Groesbeekseweg 11 6524 ck nijmegen	Paroxetine Kiron	20 mg	Coated tablet	Oral use
France	Merck Generiques 34 rue saint romain 69359 Lyon cedex 08 France	Paroxetine Merck	20 mg	Coated tablet	Oral use

France	Qualimed 34 rue saint romain 69359 Lyon cedex 08 France	Paroxetine Qualimed	20 mg	Coated tablet	Oral use
France	Ratiopharm GmbH Graf-Arco-Strasse 3 D-89079 Ulm Germany	Paroxetine Ratiopharm	20 mg	Coated tablet	Oral use
France	Laboratoire Saint-Germain 100 route de Versailles 78163 Marly-le Roy France	Paroxetine Saint Germain	20 mg / 10 ml	Oral suspension	Oral use
Germany	1 A Pharma GmbH Keltenring 1+3 82041 Oberhaching Germany	Paroxetin – 1A Pharma40 mg Filmtabletten	40 mg	Film-coated tablet	Oral use
Germany	1 A Pharma GmbH Keltenring 1+3 82041 Oberhaching Germany	Paroxetin – 1 A Pharma 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	AbZ-Pharma GmbH Dr. Georg-Spohn-Str. 7 89143 Blaubeuren Germany	Paroxetin AbZ 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	STADA Arzneimittel AG Stadastrasse 2 – 18 61118 BAD VILBEL Germany	Paroxistad 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Aliud Pharma GmbH & Co.KG Gottlieb-Daimler-Str. 19 89150 Laichingen Germany	Paroxetin AL 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use

Germany	Alpharma-ISIS GmbH & Co.KG Elisabeth-Selbert-Str. 1 40764 Langenfeld Germany	Paroxetin-Isis 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	AWD.Pharma GmbH & Co.KG Leipziger Str. 7-13 01097 Dresden Germany	Paroxetin AWD 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Sandoz Pharmaceuticals GmbH Carl-Zeiss-Ring 3 85737 Ismaning Germany	Paroxetin Sandoz 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Betapharm Arzneimittel GmbH Kobelweg 95 86156 Augsburg Germany	Paroxetin beta 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Betapharm Arzneimittel GmbH Kobelweg 95 86156 Augsburg Germany	Paroxetin beta 40 mg Filmtabletten	40 mg	Film-coated tablet	Oral use
Germany	Ct-Arzneimittel GmbH Lengeder Str. 42a 13407 Berlin Germany	Paroxetin von ct 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Henning Arzneimittel GmbH & Co.KG Liebigstr. 1-2 65439 Floersheim Germany	Depar	20 mg	Film-coated tablet	Oral use

Germany	Holsten Pharma GmbH Im Bürgerstock 7 79241 Ihringen Germany	Paroxetin Holsten	20 mg	Film-coated tablet	Oral use
Germany	IIP-Institut für industrielle Pharmazie Forschungs-und Entwicklungsgesellschaft GmbH Benzstr. 2a 63741 Aschaffenburg Germany	Osepar	20 mg	Film-coated tablet	Oral use
Germany	Esparma GmbH Lange Göhren 3 39171 Osterweddingen Germany	Aroxetin	20 mg	Film-coated tablet	Oral use
Germany	Biomo pharma GmbH Lendersberstr. 86 53721 Siegburg Germany	Paroxetin-biomo 20 mg	20 mg	Film-coated tablet	Oral use
Germany	IIP-Institut für industrielle Pharmazie Forschungs-und Entwicklungsgesellschaft GmbH Benzstr. 2a 63741 Aschaffenburg Germany	Trapar	20 mg	Film-coated tablet	Oral use
Germany	Basics GmbH Hemmelrather Weg 201 51377 Leverkusen Germany	Paroxetin Basics 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Generics (UK) Limited Station Close Potters Bar Hertfordshire EN6 1TL UK	Pasero 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use

Germany	GlaxoSmithKline GmbH & Co.KG Theresienhöhe 11 80339 München Germany	Seroxat Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	GlaxoSmithKline GmbH & Co.KG Theresienhöhe 11 80339 München Germany	Seroxat Suspension	2 mg / ml	Oral suspension	Oral use
Germany	GlaxoSmithKline GmbH & Co.KG Theresienhöhe 11 80339 München Germany	Tagonis Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	GlaxoSmithKline GmbH & Co.KG Theresienhöhe 11 80339 München Germany	Tagonis Suspension	2 mg / ml	Oral suspension	Oral use
Germany	Heumann Pharma GmbH Südwestpark 50 90449 Nürnberg Germany	Paroxetin Heumann 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Hexal AG Industriestr. 25 83607 Holzkirchen Germany	Paroc 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Hexal AG Industriestr. 25 83607 Holzkirchen Germany	Paroc 40 mg Filmtabletten	40 mg	Film-coated tablet	Oral use
Germany	Hexal AG Industriestr. 25 83607 Holzkirchen Germany	Paroxat 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use

Germany	Hexal AG Industriestr. 25 83607 Holzkirchen Germany	Paroxat 40 mg Filmtabletten	40 mg	Film-coated tablet	Oral use
Germany	Hexal AG Industriestr. 25 83607 Holzkirchen Germany	Roxac 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Hexal AG Industriestr. 25 83607 Holzkirchen Germany	Roxac 40 mg Filmtabletten	40 mg	Film-coated tablet	Oral use
Germany	Lichtenstein Pharmazeutica GmbH & Co Industrstr. 26 56218 Mulheim-Karlich Germany	ParoLich 20 Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Hexal AG Industriestr. 25 83607 Holzkirchen Germany	Paroxetin Lindo 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Hexal AG Industriestr. 25 83607 Holzkirchen Germany	Paroxetin Lindo 40 mg Filmtabletten	40 mg	Film-coated tablet	Oral use
Germany	Merck dura GmbH Frankfurter Str. 133 64293 Darmstadt Germany	Paroxedura 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Merck dura GmbH Frankfurter Str. 133 64293 Darmstadt Germany	Paroxedura 30 mg Filmtabletten	30 mg	Film-coated tablet	Oral use

Germany	Neuraxpharm Arzneimittel GmbH & Co KG Elisabeth-Selbert-Str. 23 D-40764 Langenfeld Germany	Paroxetin-neuraxpharm 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Ratiopharm GmbH Graf-Arco-Strasse 3 D-89079 Ulm Germany	Paroxetin-ratiopharm 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Ratiopharm GmbH Graf-Arco-Strasse 3 D-89079 Ulm Germany	Paroxetin-ratiopharm 30 mg Filmtabletten	30 mg	Film-coated tablet	Oral use
Germany	GlaxoSmithKline GmbH & Co.KG Theresienhöhe 11 80339 München Germany	Oxepar Suspension	2 mg / ml	Oral suspension	Oral use
Germany	GlaxoSmithKline GmbH & Co.KG Theresienhöhe 11 80339 München Germany	Paxil Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	GlaxoSmithKline GmbH & Co.KG Theresienhöhe 11 80339 München Germany	Paxil Suspension	2 mg / ml	Oral suspension	Oral use
Germany	Stadapharm GmbH Stadastr. 2-18 61118 Bad Vilbel Germany	Paroxetin STADA 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Germany	Synthon B.V. Microweg 22 NL-6545 CM Nijmegen The Netherlands	Euplix 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use

Germany	TAD Pharma GmbH Heinz-Lohmann-Str. 5 D-27472 Cuxhaven Germany	Paroxetin TAD 20 mg Filmtabletten	20 mg	Film-coated tablet	Oral use
Greece	GlaxoSmithKline A.E.B.E. 266 Kifissias Avenue 15232 Chalandri, Athens Greece	Seroxat	20 mg	Film-coated tablet	Oral use
Greece	GlaxoSmithKline A.E.B.E. 266 Kifissias Avenue 15232 Chalandri, Athens Greece	Seroxat	30 mg	Film-coated tablet	Oral use
Greece	GlaxoSmithKline A.E.B.E. 266 Kifissias Avenue 15232 Chalandri, Athens Greece	Seroxat	10 mg /5 ml	Oral suspension	Oral use
Hungary	Apotex Europe Ltd. Rowan House 41 London Street RG 14 Berkshire UK	Apodepi filmtabletta	20 mg	Film-coated tablet	Oral use
Hungary	Hexal Hungária Kft. Tímár u.20. 1034 Bp	Paretin 20 mg filmtabletta	20 mg	Film-coated tablet	Oral use
Hungary	Hexal Hungária Kft. Tímár u.20. 1034 Bp	Paretin 40 mg filmtabletta	40 mg	Film-coated tablet	Oral use
Hungary	IIP-Institut für industrielle Pharmazie F&E GmbH Benzstraße 2a D-63741 Aschaffenburg Germany	Parhun filmtabletta	20 mg	Film-coated tablet	Oral use

Hungary	Generics UK Ltd. Potters Bar EN6 1AG Hertfordshire UK	Parogen 20 mg filmabletta	20 mg	Film-coated tablet	Oral use
Hungary	Glaxo Smith Kline Kft. 1124 Bp. Csörsz u. 43. MOM Park Gesztenyés torony Hungary	Paroxat 20 mg filmtabletta	20 mg	Film-coated tablet	Oral use
Hungary	Glaxo Smith Kline Kft. 1124 Bp. Csörsz u. 43. MOM Park Gesztenyés torony Hungary	Paroxat 30 mg filmtabletta	30 mg	Film-coated tablet	Oral use
Hungary	Glaxo Smith Kline Kft. 1124 Bp. Csörsz u. 43. MOM Park Gesztenyés torony Hungary	Paroxat szirup	2 mg/ml	Syrup	Oral use
Hungary	Ratiopharm Hungary Kft. Uzsoki u. 36/A 1145 Bp Hungary	Paroxetin ratiopharm 20 mg filmtabletta	20 mg	Film-coated tablet	Oral use
Hungary	Richter Gedeon Rt. Gyömrői út 19-21. 1103 Bp Hungary	Rextine 20 mg filmtabletta	20 mg	Film-coated tablet	Oral use
Hungary	Richter Gedeon Rt. Gyömrői út 19-21. 1103 Bp Hungary	Rexetine 30 mg filmtabletta	30 mg	Film-coated tablet	Oral use
Hungary	Glaxo Smith Kline Kft. 1124 Bp. Csörsz u. 43. MOM Park Gesztenyés torony Hungary	Seroxat 20 mg tabletta	20 mg	Tablet	Oral use

Ireland	Rowex Limited, Newtown, Bantry, Co. Cork, Ireland	Paroxetine Tablets 20 mg	20 mg	Tablet	Oral use
Ireland	Rowex Limited, Newtown, Bantry, Co. Cork, Ireland	Paroxetine Tablets 40 mg	40 mg	Tablet	Oral use
Ireland	Genthon BV, Microweg 22, 6545 CM, Nijmegen, The Netherlands	Meloxat	20 mg	Film-coated tablet	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way, Rathfarnham, Dublin 16, Ireland	Paroxetine 2 mg/ml	2 mg/ml	Oral solution	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way, Rathfarnham, Dublin 16, Ireland	Paroxetine Tablets 30 mg	30 mg	Tablet	Oral use
Ireland	Norton Healthcare Limited, IVAX Quays, Albert Basin, Royal Docks London E16 2QJ, UK	Paroxetine Tablets 20 mg	20 mg	Tablet	Oral use
Ireland	Norton Healthcare Limited, IVAX Quays, Albert Basin, Royal Docks London E16 2QJ, UK	Paroxetine Tablets 30 mg	30 mg	Tablet	Oral use
Ireland	Rowex Limited, Newtown, Bantry, Co. Cork, Ireland	Parox Tablets 20 mg	20 mg	Tablet	Oral use

Ireland	GlaxoSmithKline Consumer Healthcare (Ireland) Ltd, Stonemasons Way, Rathfarnham, Dublin 16, Ireland	Seroxat Tablets 20 mg	20 mg	Tablet	Oral use
Ireland	GlaxoSmithKline Consumer Healthcare (Ireland) Ltd, Stonemasons Way, Rathfarnham, Dublin 16, Ireland	Seroxat Tablets 30 mg	30 mg	Tablet	Oral use
Ireland	GlaxoSmithKline Consumer Healthcare (Ireland) Ltd, Stonemasons Way, Rathfarnham, Dublin 16, Ireland	Seroxat Oral Suspension	20 mg / 10 ml	Oral suspension	Oral use
Iceland	Gerard Laboratories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland	Paroxetin NM Pharma	20 mg	Film-coated tablet	Oral use
Iceland	GlaxoSmithKline ehf, Thverholt 14, P.O.Box 5499, 125 Reykjavik, Iceland	Seroxat	20 mg	Tablet	Oral use
Iceland	GlaxoSmithKline ehf, Thverholt 14, P.O.Box 5499, 125 Reykjavik, Iceland	Seroxat	2 mg / ml	Mixture	Oral use

Iceland	Omega Farma ehf. Skútuvogi 1H, 104 Reykjavik, Iceland	Paroxat	10 mg	Tablet	Oral use
Iceland	Omega Farma ehf. Skútuvogi 1H, 104 Reykjavik, Iceland	Paroxat	20 mg	Tablet	Oral use
Iceland	Omega Farma ehf. Skútuvogi 1H, 104 Reykjavik, Iceland	Paroxat	30 mg	Tablet	Oral use
Iceland	Synthon BV Microweg 22 6545 CM Nijmegen The Netherlands	Euplix	20 mg	Tablet	Oral use
Italy	EG S.p.A. Via Pavia, 6 20136 Milano Italy	Paroxetina EG	20 mg	Tablet	Oral use
Italy	Abbot S.p.A. Via Pontina KM 52, 04010 Campo Verde (Aprilia), Latina Italy	Sereupin	20 mg	Tablet	Oral use
Italy	Abbot S.p.A. Via Pontina KM 52, 04010 Campo Verde (Aprilia), Latina Italy	Sereupin	2 mg/ml	Oral suspension	Oral use

Italy	GlaxoSmithKline S.p.A. Via Fleming 2 37135 Verona Italy	Seroxat	20 mg	Tablet	Oral use
Italy	GlaxoSmithKline S.p.A. Via Fleming 2 37135 Verona Italy	Seroxat	2 mg / ml	Oral suspension	Oral use
Italy	Merck Generics Italia Spa Via Aquileia 35 Cinisello Balsamo Italy	Paroxetina Merck Generics	20 mg	Film-coated tablet	Oral use
Italy	Synthon BV, Microweg 22, 6545 CM, Nijmegen, The Netherlands	Daparox	20 mg	Tablet	Oral use
Italy	Valda Laboratori Farmaceutici S.p.A. – Via Zambeletti, 20021 Baranzate Di Bollate, Milano Italy	Eutimil	20 mg	Tablet	Oral use
Italy	Valda Laboratori Farmaceutici S.p.A. Via Zambeletti, 20021 Baranzate Di Bollate, Milano Italy	Eutimil	2 mg / ml	Oral suspension	Oral use
Latvia	Medochemie Ltd P.O. Box 51409 CY-3505 Limassol Cyprus	Arketis	20 mg	Tablet	Oral use

Latvia	Glaxo Group Limited Greenford Middlesex UB6 0NN UK	Paroxat	10 mg	Coated tablet	Oral use
Latvia	Glaxo Group Limited Greenford Middlesex UB6 0NN UK	Paroxat	20 mg	Coated tablet	Oral use
Latvia	Glaxo Group Limited Greenford Middlesex UB6 0NN UK	Paroxat	30 mg	Coated tablet	Oral use
Latvia	Glaxo Group Limited Greenford Middlesex UB6 0NN UK	Seroxat	10 mg	Coated tablet	Oral use
Latvia	Glaxo Group Limited Greenford Middlesex UB6 0NN UK	Seroxat	20 mg	Coated tablet	Oral use
Latvia	Glaxo Group Limited Greenford Middlesex UB6 0NN UK	Seroxat	30 mg	Coated tablet	Oral use

Latvia	Gedeon Richter Ltd Gyomroi 19-21 H-1103 Budapest Hungary	Rexetin	20 mg	Film-coated tablet	Oral use
Latvia	Gedeon Richter Ltd Gyomroi 19-21 H-1103 Budapest Hungary	Rexetin	30 mg	Film-coated tablet	Oral use
Latvia	Hexal AG Indusstriestrasse 25 Holczkirhen D-83607 Germany	ParoxetinHexal	20 mg	Coated tablet	Oral use
Latvia	Hexal AG Indusstriestrasse 25 Holczkirhen D-83607 Germany	ParoxetinHexal	40 mg	Coated tablet	Oral use
Lithuania	Hexal AG Indusstriestrasse 25 D-83607 Holczkirhen Germany	ParoxetinHexal	20 mg	Film-coated tablet	Oral use
Lithuania	Hexal AG Indusstriestrasse 25 D-83607 Holczkirhen Germany	ParoxetinHexal	40 mg	Film-coated tablet	Oral use
Lithuania	Gedeon Richter Ltd. Gyomroi ut 19-24 1103 Budapest Hungary	Rexetin	20 mg	Film-coated tablet	Oral use

Lithuania	Gedeon Richter Ltd. Gyomroi ut 19-24 1103 Budapest Hungary	Rexetin	30 mg	Film-coated tablet	Oral use
Lithuania	SmithKline Beecham plc SB House, Great West road, Brentford, Middlesex, UK	Seroxat	20 mg	Film-coated tablet	Oral use
Lithuania	SmithKline Beecham plc SB House, Great West road, Brentford, Middlesex, UK	Seroxat	30 mg	Film-coated tablet	Oral use
Luxembourg	GlaxoSmithKline s.a./n.v. Rue du Tilleul, 13 B-1332 Genval Belgium	Aropax	20 mg	Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a./n.v. Rue du Tilleul, 13 B-1332 Genval Belgium	Aropax	30 mg	Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a./n.v. Rue du Tilleul, 13 B-1332 Genval Belgium	Aropax	20 mg/10 ml	Oral suspension	Oral use
Luxembourg	GlaxoSmithKline s.a./n.v. Rue du Tilleul, 13 B-1332 Genval Belgium	Seroxat	20 mg	Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a./n.v. Rue du Tilleul, 13 B-1332 Genval Belgium	Seroxat	30 mg	Tablet	Oral use

Luxembourg	GlaxoSmithKline s.a./n.v. Rue du Tilleul, 13 B-1332 Genval Belgium	Seroxat	20 mg /10 ml	Oral suspension	Oral use
Luxembourg	Merck s.a., 288 Brusselsesteenweg, B-3090 Overijse Belgium	Merck-Paroxetine 20 mg	20 mg	Tablet	Oral use
Malta	Smithkline Beecham Plc SB House Great West Road Bentford TW8 9BD Middlesex United Kingdom	Seroxat	20 mg	Coated tablet	Oral use
Malta	Actavis hf Reykjavikurvegur 78 220 Hafnarfjordur Iceland	Paxetin	20 mg	Tablet	Oral use
The Netherlands	Centrafarm Services B.V., Nieuwe Donk 9, P.O.Box 289, 4870 Ag Etten-Leur, The Netherlands	Paroxetine CF 20 mg	20 mg	Tablet	Oral use
The Netherlands	Genthon BV Box 7071 GN NIJMEGEN The Netherlands	Paroxetine 20 mg	20 mg	Film-coated tablet	Oral use
The Netherlands	GlaxoSmithKline BV, Huister Heideweg 62, P.O.Box 780, 3700 At Zeist The Netherlands	Seroxat Suspensie 2 mg / ml	2 mg/ml	Oral suspension	Oral use

The Netherlands	GlaxoSmithKline BV, Huister Heideweg 62, P.O.Box 780, 3700 At Zeist The Netherlands	Seroxat 20 mg tablets	20 mg	Tablet	Oral use
The Netherlands	GlaxoSmithKline BV, Huister Heideweg 62, P.O.Box 780, 3700 At Zeist The Netherlands	Seroxat 30 mg tablets	30 mg	Film-coated tablet	Oral use
The Netherlands	Hexal Pharma Nederland B.V. Pastoorslaan 28, P.O.Box 251 2182 Bx Hillegom, The Netherlands	Paroxetine 20 mg	20 mg	Film-coated tablet	Oral use
The Netherlands	Hexal Pharma Nederland B.V. Pastoorslaan 28, P.O.Box 251 2182 Bx Hillegom, The Netherlands	Paroxetine 40 mg	40 mg	Film-coated tablet	Oral use
The Netherlands	I.C.C. BV P.O.Box 75 6920 Ab Duiven The Netherlands	Paroxetine 20 mg	20 mg	Tablet	Oral use
The Netherlands	Merck Generics BV, Dieselweg 25, NL-3752 Lb Bunschoten, The Netherlands	Paroxetine Merck 20 mg	20 mg	Tablet	Oral use
The Netherlands	Multipharma BV, Gemeenschapspolderweg 28 P.O.Box 216 1382 Gr Weesp The Netherlands	MP-Paroxetine 20 mg	20 mg	Film-coated tablet	Oral use

Norway	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroxetine Gea	20 mg	Film-coated tablet	Oral use
Norway	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Demark	Paroxetine Gea	40 mg	Film-coated tablet	Oral use
Norway	Sandoz GmbH, Biochemiestrasse 10, A-6250 Kundl, Austria	Paroxetin Biochemie	20 mg	Film-coated tablet	Oral use
Norway	Duranor AS, Oslo, Norway	Serodur	20 mg	Tablet	Oral use
Norway	GlaxoSmithKline AS, Forskningsveien 2a, Postbox 180 Vinderen, N-0319, Oslo, Norway	Seroxat	20 mg	Tablet	Oral use
Norway	NM Pharma AS, Lilleakerveien, 2B, Oslo, Norway	Paroxetin NM Pharma	20 mg	Film-coated tablet	Oral use
Norway	Ratiopharm GmbH, Graf-Acro-Strasse 3, D-89079 Ulm, Germany	Paroxetin Ratiopharm	20 mg	Film-coated tablet	Oral use
Norway	STADA Arzneimittel AG, Stadastrasse 2 – 18, 61118 BAD VILBEL, Germany	Paroxetin Stada	20 mg	Film-coated tablet	Oral use

Poland	Apotex Inc. ul. Homera 46, 04-624 Warsaw Poland	Apo-Parox 20	20 mg	Film-coated tablet	Oral use
Poland	Pliva Kraków Zakłady Farmaceutyczne S.A. ul. Mogilska 80, 31-546 Cracow. Poland	Deprozel 20 mg	20 mg	Film-coated tablet	Oral use
Poland	ratiopharm GmbH Graf-Arco-Strasse 3 89079 Ulm, Germany	Paxeratio	20 mg	Film-coated tablet	Oral use
Poland	Gedeon Richter Ltd. H-1103 Budapest, Gyömrōi ut 19-21, Hungary	Rexetin	20 mg	Film-coated tablet	Oral use
Poland	GlaxoSmithKline Export Ltd. 980 Great West Road Brentford, Middlesex, TW8 9GS UK	Seroxat	20 mg	Film-coated tablet	Oral use
Poland	GlaxoSmithKline Export Ltd. 980 Great West Road Brentford, Middlesex, TW89GS UK	Seroxat	30 mg	Film-coated tablet	Oral use
Poland	Hexal Polska Sp. z o.o. ul Domaniewska 50C 02-672 Warsaw Poland	Paxtin 20	20 mg	Film-coated tablet	Oral use
Poland	Hexal Polska Sp. z o.o. ul Domaniewska 50C 02-672 Warsaw Poland	Paxtin 40	40 mg	Film-coated tablet	Oral use

Portugal	Jaba Farmacêutica, S.A. Edifício Jaba – Rua da Tapada Grande, 2 – Zona Industrial da Abrunheira 2710-089 Sintra	Denerval	20 mg	Film-coated tablet	Oral use
Portugal	Alpharma ApS Rua Virgílio Correia, 11-A 1600-219 Lisboa Portugal	Paroxetina Alpharma 20 mg Comprimidos	20 mg	Film-coated tablet	Oral use
Portugal	Biara – Produtos Farmacêuticos, Lda. Rua Ramalho Ortigão, 45-A, 1070-228 Lisboa Portugal	Paroxetina Biara 20 mg Comprimidos Revestidos	20 mg	Film-coated tablet	Oral use
Portugal	Sandoz GmbH Biochemiestraße 10, A-6250 Kundl Austria	Paroxetina Sandoz 20 mg Comprimidos	20 mg	Film-coated tablet	Oral use
Portugal	Farma APS – Produtos Farmacêuticos, S.A. Rua José Galhardo nº. 3, loja 3 - C/v 1750-131 Lisboa Portugal	Paroxetina APS 20 mg Comprimidos Revestidos	20 mg	Film-coated tablet	Oral use
Portugal	Bexal Produtos Farmacêuticos S.A. Rua Prof. Ricardo Jorge, 5 A-Miraflores 1495-153 Algés	Paroxetina Bexal 20 mg Comprimido revestido por película	20 mg	Film-coated tablet	Oral use
Portugal	Generis Farmacêutica, S.A. Rua José Galhardo nº. 3, 1750-131 Lisboa Portugal	Paroxetina Generis 20 mg Comprimidos Revestidos	20 mg	Film-coated tablet	Oral use

Portugal	GlaxoSmithkline Produtos Farmacêuticos, Lda. Rua Dr. António Loureiro Borges, 3, Arquiparque – Miraflores 1495-131 Algés	Seroxat	20 mg	Film-coated tablet	Oral use
Portugal	GlaxoSmithkline Produtos Farmacêuticos, Lda. Rua Dr. António Loureiro Borges, 3, Arquiparque Miraflores 1495-131 Algés	Seroxat	2 mg / ml	Oral suspension	Oral use
Portugal	Instituto Luso-Fármaco, Lda. Rua Dr. António Loureiro Borges, 3, Arquiparque – Miraflores 1495-131 Algés	Calmus	20 mg	Film-coated tablet	Oral use
Portugal	Laboratórios Azevedos – Indústria Farmacêutica, S.A. Estrada Nacional 117-2 2724-503 Alfragide	Oxepar	20 mg	Film-coated tablet	Oral use
Portugal	Instituto Luso-Fármaco, Lda. Rua Dr. António Loureiro Borges, 3, Arquiparque – Miraflores 1495-131 Algés	Oxepar	2 mg / ml	Oral suspension	Oral use
Portugal	Medibial – Produtos Médicos e Farmacêuticos, S.A, Av. Da Siderurgia Nacional, 4745-457 S. Mamede do Coronado	Paxetil	20 mg	Film-coated tablet	Oral use
Portugal	Medibial – Produtos Médicos e Farmacêuticos, S.A, Av. Da Siderurgia Nacional, 4745-457 S. Mamede do Coronado	Paxetil	2 mg / ml	Oral suspension	Oral use

Portugal	Merck Genéricos – Produtos Farmacêuticos, Lda. Rua Alfredo da Silva, 3 – C, P-1300-040 Lisboa Portugal	Paroxetina Merck Genericos 20 mg Comprimidos Revestidos	20 mg	Film-coated tablet	Oral use
Portugal	Merck S.A, Rua Alfredo da Silva, 3-C, P-1300-040 Lisboa Portugal	Paxpar	20 mg	Film-coated tablet	Oral use
Portugal	Ratiopharm - Comércio e Indústria de Produtos Farmacêuticos, Lda. Edifício Tejo - 6° Piso - Rua Quinta do Pinheiro 2790-143 Carnaxide	Paroxetina Ratiopharm 20 mg Comprimidos	20 mg	Film-coated tablet	Oral use
Portugal	Synthon B.V. Microweg 22, 6545 CM Nijmegen The Netherlands	Parox	20 mg	Film-coated tablet	Oral use
Portugal	Tecnimede – Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros Edifício Sagres, 3° A 2685-338 Prior Velho	Paroxetina Tecnimede 20 mg Comprimidos Revestidos	20 mg	Film-coated tablet	Oral use
Slovac Republic	Generics UK Ltd. Station Close, Potters Bar, Herts EN6 1TL UK	Paretin 20mg	20 mg	Film-coated tablet	Oral use
Slovac Republic	A/S GEA Farmaceutisk Fabrik Holger Danskaes Vej 89 2000 Fraderiksberg Denmark	Parolex 20	20 mg	Film-coated tablet	Oral use

Slovac Republic	A/S GEA Farmaceutisk Fabrik Holger Danskaes Vej 89 2000 Fraderiksberg Denmark	Parolex 40	40 mg	Film-coated tablet	Oral use
Slovac Republic	ratiopharm GmbH Gras-Orco-Strasse 3 89079 Ulm	Paroxetini-ratiopharm 20mg	20 mg	Film-coated tablet	Oral use
Slovac Republic	Gedeon Richter Ltd. Gyomroi út 19-21 1103 Budapest Hungary	Remood 20 mg	20 mg	Film-coated tablet	Oral use
Slovac Republic	Gedeon Richter Ltd. Gyomroi út 19-21 1103 Budapest Hungary	Remood 30 mg	30 mg	Film-coated tablet	Oral use
Slovac Republic	SmithKlineBeecham Pharmaceuticals 980 Great West Road Brentford Middlesex TW8 9GS UK	Seroxat 20 mg tbl flm	20 mg	Film-coated tablet	Oral use
Slovac Republic	SmithKlineBeecham Pharmaceuticals 980 Great West Road Brentford Middlesex TW8 9GS UK	Seroxat 30 mg tbl flm	30 mg	Film-coated tablet	Oral use

Slovenia	GlaxoSmithKline d.o.o., družba za promet s farmacevtskimi izdelki, Knezov štradon 90, Ljubljana Slovenia	Paroxat	20 mg	Film-coated tablet	Oral use
Slovenia	GlaxoSmithKline d.o.o., družba za promet s farmacevtskimi izdelki, Knezov štradon 90, Ljubljana Slovenia	Paroxat	30 mg	Film-coated tablet	Oral use
Slovenia	GlaxoSmithKline d.o.o., družba za promet s farmacevtskimi izdelki, Knezov štradon 90, Ljubljana Slovenia	Seroxat	20 mg	Film-coated tablet	Oral use
Slovenia	GlaxoSmithKline d.o.o., družba za promet s farmacevtskimi izdelki, Knezov štradon 90, Ljubljana Slovenia	Seroxat	30 mg	Film-coated tablet	Oral use
Slovenia	Merck, Proizvodnja in prodaja farmacevtskih in kemijskih proizvodov, d.o.o., Dunajska 156, Ljubljana Slovenia	Parogen	20 mg	Film-coated tablet	Oral use
Sweden	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroxetine GEA	20 mg	Film-coated tablet	Oral use
Sweden	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroxetine GEA	40 mg	Film-coated tablet	Oral use
Sweden	Alpharma AS, P.O. Box 158, Skoyen, N-0212 Oslo, Norway	Paroxetin Alpharma	20 mg	Film-coated tablet	Oral use

Sweden	AWD. Pharma GmbH & Co. KG Leipziger Str. 7-13 01097 Dresden Germany	Paroximed	20 mg	Film-coated tablet	Oral use
Sweden	Gerard Laboratiories, 35/36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland	Paroxetin Scand Pharm	20 mg	Film-coated tablet	Oral use
Sweden	GlaxoSmithKline AB, Box 263, SE-431 23 Mölndal, Sweden	Seroxat	20 mg	Film-coated tablet	Oral use
Sweden	GlaxoSmithKline AB, Box 263, SE-431 23 Mölndal, Sweden	Seroxat	2 mg /ml	Oral suspension	Oral use
Sweden	GlaxoSmithKline AB, Box 263, SE-431 23 Mölndal, Sweden	Paroxetin ratiopharm	20 mg	Film-coated tablet	Oral use
Sweden	GlaxoSmithKline AB, Box 263, SE-431 23 Mölndal, Sweden	Paroxat	20 mg	Film-coated tablet	Oral use
Sweden	GlaxoSmithKline AB, Box 263, SE-431 23 Mölndal, Sweden	Meradel	20 mg	Tablet	Oral use
Sweden	GlaxoSmithKline AB, Box 263, SE-431 23 Mölndal, Sweden	Eoxat	20 mg	Tablet	Oral use

Sweden	Heumann Pharma GmbH, Südwestpark 50, 90449 Nürnberg, Germany	Deoxatine 20 mg Filmdragerade tabletter	20 mg	Film-coated tablet	Oral use
Sweden	Lichtenstein Pharmazeutica GmbH & Co. Industrstr. 26 56218 Mulheim-Karlich Germany	Mediparox	20 mg	Film-coated tablet	Oral use
Sweden	Medis-Danmark A/S Havelse Molle 14 DK-3600 Frederikssund Denmark	Paroxetin ”Medis”	20 mg	Film-coated tablet	Oral use
Sweden	Medis-Danmark A/S Havelse Molle 14 DK-3600 Frederikssund Denmark	Paroxetabs	20 mg	Film-coated tablet	Oral use
Sweden	Medis-Danmark A/S Havelse Molle 14 DK-3600 Frederikssund Denmark	Parotamed	20 mg	Film-coated tablet	Oral use
Sweden	Medis-Danmark A/S Havelse Molle 14 DK-3600 Frederikssund Denmark	Paraxodil	20 mg	Film-coated tablet	Oral use
Sweden	Medis-Danmark A/S Havelse Molle 14 DK-3600 Frederikssund Denmark	Primoxatine	20 mg	Film-coated tablet	Oral use
Sweden	Medis-Danmark A/S Havelse Molle 14 DK-3600 Frederikssund Denmark	Titroxatine	20 mg	Film-coated tablet	Oral use

Sweden	Neuraxpharm Arzneimittel GmbH & Co. KG Elisabeth-Selbert-Str. 23 D-40764 Langenfeld Germany	Isoxatine	20 mg	Film-coated tablet	Oral use
Sweden	Ratiopharm GmbH, Graf-Arco-Strasse 3, D-89079 Ulm, Germany	Paroxin	20 mg	Film-coated tablet	Oral use
Sweden	STADA Arzneimittel AG, Stadastrasse 2 – 18, 61118 Bad Vilbel, Germany	Parocetan	20 mg	Film-coated tablet	Oral use
Sweden	STADA Arzneimittel AG, Stadastrasse 2 – 18, 61118 Bad Vilbel, Germany	Paroxiflex	20 mg	Film-coated tablet	Oral use
Sweden	STADA Arzneimittel AG, Stadastrasse 2 – 18, 61118 Bad Vilbel, Germany	Paroxistad	20 mg	Film-coated tablet	Oral use
Sweden	Synthon BV, Microweg 22, 6545 CM Mijmegen, The Netherlands	Euplix	20 mg	Film-coated tablet	Oral use
Sweden	TAD Pharma GmbH, Heinz-Lohmann-Strasse 5, 27472 Cuxhaven, Germany	Medoxatine	20 mg	Film-coated tablet	Oral use
Spain	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg	Paroxetina Gea 20 mg	20 mg	Film-coated tablet	Oral Use

Spain	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroxetina Gea 40 mg	40 mg	Film-coated tablet	Oral use
Spain	Bexal Farmaceutica S.A. Ventura Rodriguez 7, 5 planta 28008 Madrid Spain	Paroxetina Bexal 20 mg comprimidos EFG	20 mg	Film-coated tablet	Oral use
Spain	Laboratorios Davur S.L. Teide, 4-planta baja Poligono Empresarial La Marina 28700 San Sebastian de los Reyes, Madrid Spain	Paroxetina Davur 20 mg Comprimidos Recubiertos EFT	20 mg	Coated tablet	Oral use
Spain	Faes Farma S.A. Maximo Aguirre 14, 48940 Lejona (Vizcaya)	Motivan 20 mg, comprimidos	20 mg	Film-coated tablet	Oral use
Spain	Laboratorios Fournier S.A. Ronda de Poniente 16 28760-Tres Cantos, Madrid Spain	Casbol 20 mg comprimidos con cubierta pelicular	20 mg	Film-coated tablet	Oral use
Spain	GlaxoSmithKline S.A. Severo Ochoa 2 28760 Tres Cantos, Madrid Spain	Seroxat 20 mg comprimidos con cubierta pelicular	20 mg	Film-coated tablet	Oral use
Spain	Laboratorios Alter S.A. Mateo Inurria 30 28036 Madrid Spain	Paroxetina Alter 20 mg comprimidos con cubierta pelicular	20 mg	Film-coated tablet	Oral use

Spain	Laboratorios Belmac S.A. Teide, 4-planta baja Poligono Empresarial La Marina 28700 San Sebastián de los Reyes, Madrid Spain	Xetin 20 mg comprimidos recubiertos	20 mg	Coated tablet	Oral use
Spain	Merck Genericos S.L. Ctra.n-152 Km 19 – Poligono Merck 08100 Mollet del Valles, Barcelona Spain	Paroxetina Merck 20 mg Comprimidos recubiertos EFG	20 mg	Coated tablet	Oral use
Spain	Mundogen Farma S.A. Severo Ochoa, 2 Parque Tecnológico de Madrid 28760 Tres Cantos Madrid	Paroxetina Mundogen 20 mg comprimidos con cubierta pelicular EFG	20 mg	Film-coated tablet	Oral use
Spain	Novartis Farmaceutica S.A. Gran Via de les Corts Catalanes 764 08013 Barcelona Spain	Frosinor 20 mg Comprimidos con cubierta pelicular	20 mg	Film-coated tablet	Oral use
Spain	Ratiopharm España S.A. Avda. De Burgos, 16D – 5a planta 28036 Madrid Spain	Paroxetina ratiopharm 20 mg comprimidos recubiertos EFT	20 mg	Coated tablet	Oral use
Spain	Laboratorios Rimafar S.L. Pololigono Malpica Calle c, No 4 50016 Zaragoza	Paroxetina Rimafar 20 mg comprimidos recubiertos EFT	20 mg	Coated tablet	Oral use
Spain	Synthon BV Microweg 22 NL 6545 CM Nijmegen The Netherlands	Paroxetina Synthon	20 mg	Film-coated tablet	Oral use

Spain	Tamarang S.A. Balmes, 84-4-2a 08008 Barcelona Spain	Paroxetina Tamarang	20 mg	Coated tablet	Oral use
Spain	Tamarang S.A. Balmes, 84-4-2a 08008 Barcelona Spain	Paroxetina Apotex-Farma	20 mg	Coated tablet	Oral use
United Kingdom	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Denmark	Paroxetine 20 mg Tablet	20 mg	Tablet	Oral use
United Kingdom	A/S GEA Farmaceutisk Fabrik Holger Danskes Vej 89 DK-2000 Frederiksberg Demark	Paroxetine 40 mg Tablet	40 mg	Tablet	Oral use
United Kingdom	Alpharma Ltd; Whiddon Valley; Barnstaple; N. Devon EX32 8NS, UK	Paroxetine 20 mg Tablet	20 mg	Tablet	Oral use
United Kingdom	Alpharma Ltd; Whiddon Valley; Barnstaple; N. Devon EX32 8NS, UK	Paroxetine 30 mg Tablet	30 mg	Tablet	Oral use
United Kingdom	Apotex Europe Limited; Rowan House; 41 London street; Reading; Berkshire RG1 4PS UK	Paroxetine 20 mg Tablet	20 mg	Tablet	Oral use

United Kingdom	Generics (UK) Limited; Station Close; Potters Bar; Hertfordshire EN6 1TL, UK	Paroxetine 20 mg Film-coated tablet	20 mg	Film-coated tablet	Oral use
United Kingdom	GlaxoSmithKline UK Limited Stockley Park West Uxbridge Middlesex UB11 1BT UK	Seroxat Tablets 20 mg	20 mg	Tablet	Oral use
United Kingdom	GlaxoSmithKline UK Limited Stockley Park West Uxbridge Middlesex UB11 1BT UK	Seroxat Tablers 30 mg	30 mg	Tablet	Oral use
United Kingdom	GlaxoSmithKline UK Limited Stockley Park West Uxbridge Middlesex UB11 1BT UK	Seroxat Liquid 20 mg/10ml	2 mg / ml	Oral suspension	Oral use
United Kingdom	GlaxoSmithKline UK Limited Stockley Park West Uxbridge Middlesex UB11 1BT UK	Paroxetine Hydrochloride Tablets 20 mg	20 mg	Tablet	Oral use

United Kingdom	GlaxoSmithKline UK Limited Stockley Park West Uxbridge Middlesex UB11 1BT UK	Paroxetine Hydrochloride Tablets 30 mg	30 mg	Tablet	Oral use
United Kingdom	GlaxoSmithKline UK Limited Stockley Park West Uxbridge Middlesex UB11 1BT UK	Paroxetine Hydrochloride Liquid 20mg/10ml	2 mg/ml	Oral suspension	Oral use
United Kingdom	Lagap Pharmaceuticals Ltd; Woolmer Way; Bordon; Hampshire GU35 9QE, UK	Paroxetine 20 mg Tablet	20 mg	Tablet	Oral use
United Kingdom	Medis-Danmark A/S Havelse Molle 14 DK-3600 Frederikssund Danmark	Paroxetine 20 mg Tablet	20 mg	Tablet	Oral use
United Kingdom	Norton Healthcare Limited; IVAX Quays, Albert Basin, Royal Docks, London E16 2QJ, UK	Paroxetine Hydrochloride Tablets 20 mg	20 mg	Tablet	Oral use
United Kingdom	Ratiopharm GmbH, Graf-Arco-Strasse 3, D-89079 Ulm, Germany	Paroxetine 20 mg tablets	20 mg	Tablet	Oral use

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARIES OF PRODUCT CHARACTERISTICS PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF PAROXETINE CONTAINING MEDICINAL PRODUCTS (see Annex I)

Paroxetine is a phenylpiperidine derivative and is a potent and selective inhibitor of the presynaptic 5-hydroxytryptamine (5-HT) reuptake. Paroxetine inhibits the neuronal uptake of serotonin and thereby facilitates serotonergic transmission. Paroxetine was first approved in 1990 as an antidepressant in the U.K. Subsequently paroxetine has been approved for the treatment of various psychiatric disorders in all EU Member States. The indications for which paroxetine is currently approved in EU includemajor depressive disorder (MDD), panic disorder, obsessive compulsive disorder (OCD), social phobia/social anxiety disorder (SAD), generalised anxiety disorder (GAD) and post-traumatic stress disorder (PTSD).

There has been a concern about withdrawal reactions associated with paroxetine since its licensing. Clinical trials, which have included gradual dose reduction at the end of treatment, have found that 30% of patients developed symptoms following discontinuation of treatment with paroxetine compared to 20% among those stopping placebo. Although the majority of the symptoms reported in the clinical trials were not serious and not described as severe, subsequently there was evidence from spontaneous reports that some patients experienced serious and severe symptoms on stopping paroxetine.

The issue of suicidal behaviour among patients treated with paroxetine has been addressed in the past in literature and at national level in some Member States. In May 2003 UK reviewed data from clinical trials with paroxetine in the treatment of paediatric OCD, SAD and MDD and concluded that these data provided evidence of an association between the use of paroxetine and an increased risk of emotional lability including self-harm, hostility and suicidal behaviour in children and adolescents. Various analyses suggested that the risk of these outcomes was between 1.5 and 3.2 times greater with paroxetine compared to placebo. In addition, efficacy could not be demonstrated in this population. In response to these data UK contraindicated the use of paroxetine in children aged 18 years or less with major depressive disorders.

On 13 June 2003, UK triggered a referral to the EMEA under Article 31 of Directive 2001/83/EC, as amended, to medicinal products containing paroxetine. Based on the above data concerning withdrawal reactions and suicidal behaviour, UK considered that there was Community interest to reassess the balance of risks and benefits of paroxetine and requested the CHMP to give an opinion on whether the marketing authorisations for paroxetine containing medicinal products should be maintained, varied or withdrawn.

EFFICACY

A discussion on the efficacy of paroxetine containing medicinal products took place in CHMP based on the Rapporteur´s and Co-Rapporteur´s Assessment Reports and the data presented by the Marketing Authorisation Holders (MAHs).

Efficacy in adults

Major Depressive Episode

The efficacy of paroxetine in treating major depression in adults is established and supported by numerous short and long-term trials. The long-term efficacy of paroxetine in depression has been demonstrated in a 52 week maintenance study with relapse prevention design: 12% of patients receiving paroxetine (20-40mg daily) relapsed, versus 28% of patients on placebo.

Obsessive Compulsive Disorder

The efficacy of paroxetine in treating OCD in adults was investigated in short-term and long-term studies. Significant and relevant results were obtained in some of the short-term studies. The long-term

efficacy of paroxetine in treating OCD was examined in three 24 week maintenance studies with relapse prevention design. One of the three studies achieved a significant difference in the proportion of relapsers between paroxetine (38%) compared to placebo (59%).

Panic Disorder

The efficacy of paroxetine in the treatment of panic disorders in adults was investigated in some short-term and long-term studies. Significant and relevant results were obtained in some of these studies. The long-term efficacy of paroxetine in treating panic disorder was demonstrated in a 24 week maintenance study with relapse prevention design: 5% of patients receiving paroxetine (10-40mg daily) relapsed, versus 30% of patients on placebo. This was supported by a 36 week maintenance study.

Social Anxiety Disorder / Social Phobia

The efficacy of paroxetine in the treatment of social anxiety disorders in adults was investigated in some short-term and long-term studies. Significant and relevant results were obtained in the short-term studies but not in the long-term studies and therefore the CHMP concluded that the long-term efficacy has not been sufficiently demonstrated.

Generalised Anxiety Disorder

The efficacy of paroxetine in the treatment of GAD in adults was investigated in some short-term and long-term studies. Significant and relevant results were obtained in the short-term but not in the long-term studies and therefore the CHMP concluded that the long-term efficacy has not been sufficiently demonstrated.

Post-traumatic Stress Disorder

The efficacy of paroxetine in the treatment of PTSD in adults was investigated in some short-term and long-term studies. The CHMP considered that despite some problems in the studies, mainly related to the fact that many patients suffered from co-morbid depression, there is evidence to support the efficacy in this indication, however the long-term efficacy has not been sufficiently demonstrated.

On the basis of the assessed data the CHMP concluded that paroxetine is effective in the treatment of major depressive episode, obsessive compulsive disorder, panic disorder with and without agarophobia, social anxiety disorder/social phobia, generalised anxiety disorder and post-traumatic stress disorder. The CHMP also agreed that the above-mentioned information with regards to long-term efficacy should be included in section 5.1 (Pharmacodynamic Properties) of the Summary of Product Characteristics (SPC).

Posology

The CHMP also considered the available data supporting the recommended posology for each of the above indications. The recommended daily dose of paroxetine is 40mg/day for OCD and panic disorder and 20mg/day for the other indications. The CHMP discussed in particular whether higher doses may be necessary for some patients and can be justified by the available data. From the data provided the CHMP noted that in the fixed dose studies there was a flat dose response curve, providing no suggestion of advantage in terms of efficacy for using higher than the recommended doses. However, there is some clinical data suggesting that up-titrating the dose might be beneficial for some patients.

On the basis of the available data the CHMP concluded that if after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose gradually increased (in 10 mg steps) up to a maximum of 50mg/day for MDD, SAD, GAD and PTSD and up to a maximum of 60mg/day for OCD and panic disorder. Therefore the CHMP recommended that section 4.2 (Posology and Method of Administration) of the SPC should be amended accordingly. In addition, the CHMP agreed that information with regards to the dose response studies should be included in section 5.1 (Pharmacodynamic Properties) of the SPC.

Efficacy in children

Currently paroxetine is not authorised for use in children and adolescents in any EU Member State. From the data provided by the MAHs the CHMP concluded that efficacy has not been demonstrated in children and adolescents with major depressive disorder as included in the trials. Insufficient evidence has been made available concerning the efficacy of paroxetine for the treatment of obsessive compulsive disorder and social anxiety/social phobia. According to the answers provided by the MAHs to CHMP, no studies were performed in children and adolescents in the other currently approved indications for adults. No long-term data were submitted.

SAFETY

The overall safety profile of paroxetine containing medicinal products was reviewed by the CHMP. A discussion on the safety of paroxetine containing medicinal products took place in CHMP based on the Rapporteur´s and Co-Rapporteur´s Assessment Reports and the data presented by the MAHs. The main safety issues discussed were the risk of suicide and the risk of withdrawal reactions.

Suicidal behaviour, self-harm and hostility

Adults

Based on the assessment of data from clinical trials and from post marketing the CHMP concluded that there is a possibility of an increased risk of suicidal related behaviour associated with paroxetine in young adults (18-29 years), even though the increased risk was not statistically significant.

In the older age groups no such increase was observed. Results from observational studies indicate no increased risk of suicidality in patients who were prescribed paroxetine and likewise, post marketing reports indicate low rates of suicidal related behaviours. Clinical trials show similar low rates in placebo and paroxetine treated depressed patients. Rates in patients with other disorders for which paroxetine is indicated are similarly low.

Children and adolescents

Overall data from clinical trials indicate an increased risk of suicidal and hostility related behaviours in the paediatric population (7-17 years old). The incidence of possible suicide-related events and self-harm in the paroxetine group were 2-3 times that seen in the placebo group, while hostility events in the paroxetine occurred with a frequency 6 times that seen in the placebo group. Suicidal related behaviours associated with paroxetine in the clinical trials were more clearly seen in the depression studies than in studies of OCD or SAD. Hostility events were more clearly seen in the OCD studies than in the depression studies. In view of these findings the CHMP considered that a statement advising that paroxetine should not be used in children and adolescents should be included in section 4.4 (Special Warnings and Special Precautions for Use) of the SPC and that information on the adverse events from paediatric clinical trials should be included in section 4.8 (Undesirable Effects) of the SPC.

New data available after the CHMP Opinion of 22 April 2004: GPRD studies

During the decision-making process for the article 31 referral on paroxetine subsequent to the CHMP opinion of 22 April 2004, UK informed the European Commission that three new studies with direct relevance to this issue had become available. Further to a meeting of the Standing Committee the Commission requested the CHMP to review the new available data.

These new data reviewed by CHMP included three studies (one published and two unpublished) based on the UK General Practice Research Database (GPRD). These studies investigated the risk of suicidal behaviours (including completed suicides, suicide attempts and suicidal ideation) associated with the use of various antidepressants. Although all three analyses derived their data from the same database, they differed in a certain extent from each other in terms of design, definitions, specific products that were compared and the time frame within which patients' data was examined. In essence similar

methods were employed in examining differences in risk of suicidal events among GP (General Practitioner) patients treated with different antidepressants.

For adults, all three studies showed no significant difference in risk for suicidal behaviours among patients receiving different antidepressants or antidepressants of different classes (i.e. Tricyclic antidepressants – TCA - vs. SSRI vs. other antidepressants). For children and adolescents, although no completed suicides were observed, an increased risk for suicidal and self-harm behaviours was observed in patients taking SSRIs compared to those taking TCAs and in patients taking paroxetine compared to those taking other SSRIs. These studies did not show a statistical significant elevation of suicide related events and self harm in young adults. Furthermore in one of the studies the relation between suicidality risk in relation to the indication was investigated. In accordance to the results, the association between suicidality risk and paroxetine appears significant only among patients with previous depression but not among patients with previous depression and anxiety or anxiety alone.

On the basis of the new assessed data the CHMP concluded the following:

- The new evidence from the GPRD studies is more vulnerable to various biases, e.g. confounding by indication, compared to evidence coming from clinical trials. Therefore, although data from the GPRD studies apparently do not confirm the findings from clinical trials with respect to increased risk in patients with anxiety disorders or in young adults, the fact that these risks were found in clinical trials justifies a warning in the SPC in relation to the risk of suicide/suicidal ideation in children and adolescents irrespective of the indication and a warning for young adults.
- Increased suicidal related behaviours in children and adolescents was already seen in the clinical trials and post-marketing data and therefore the CHMP did not consider that the new data added new evidence on this regard.

In view of the above the CHMP confirmed its previous conclusions in relation to the risk of suicidal behaviour in patients using paroxetine. Therefore, the CHMP concluded that the previous agreed statement advising that paroxetine should not be used in children and adolescents included in section 4.4 (Special Warnings and Special Precautions for Use) of the SPC and the warning in relation to young adults should remain unchanged.

Withdrawal reactions

Adults

Available data from clinical trials, spontaneous reports and published literature show that withdrawal reactions in association with paroxetine are common when treatment is discontinued. In clinical trials adverse events seen on treatment discontinuation occurred in 30% of patients treated with paroxetine compared to 20% of patients treated with placebo.

The most commonly reported adverse events are dizziness, sensory disturbances, sleep disturbances, anxiety and headache. Other withdrawal reactions that have been reported on discontinuation of paroxetine include agitation, nausea, tremor, confusion, sweating, diarrhoea, palpitations, emotional instability, irritability and visual disturbances. In general these events are mild to moderate, occur within the first week of cessation of treatment and resolve within two weeks. However, in a significant proportion of individuals they may be severe in intensity and of prolonged duration (2-3 months or more). From the assessed data there was no indication of a signal of dependence with paroxetine.

Analysis of the available data from clinical trials and spontaneous reporting data indicate that the risk of withdrawal reactions is dependent on several factors including the duration and dose of therapy and the rate of dose reduction. Therefore, patients treated with higher doses, those treated for a longer duration and patients whose treatment is abruptly stopped may be at an increased risk of withdrawal symptoms upon stopping treatment with paroxetine.

In view of these conclusions the CHMP considered that guidance with regards to the discontinuation of paroxetine (down titration), as well as a warning and a description of the withdrawal symptoms seen on discontinuation of paroxetine should be included in the respective sections of the SPC and suitable pharmaceutical forms/strengths need to be available in order to facilitate titration.

Children and adolescents

In clinical trials 28% of patients treated with paroxetine reported withdrawal symptoms compared with 19% of placebo treated patients. The most common withdrawal symptoms in children and adolescents were headaches, dizziness, nausea, nervousness and abdominal pain. Most withdrawal symptoms were mild or moderate. None required re-start of the medication. There was no indication of a signal of dependence of paroxetine, but long-term data are not available.

Pregnancy/Neonates

The CHMP reviewed available data from published literature and spontaneous reports in relation to withdrawal reactions in neonates whose mothers used paroxetine during pregnancy. Symptoms such as respiratory distress, cyanosis, apnoea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycaemia, hypertonia, hypotonia, hyperreflexia, tremor, jitteriness, irritability, lethargy, constant crying, somnolence and difficulty in sleeping may occur.

On the basis of the available data the CHMP considered that the above information on the symptoms which can occur in the neonate after maternal paroxetine use in later stages of pregnancy, should be included in section 4.6 (Pregnancy and Lactation) of the SPC.

Akathisia

Available data, including data from clinical trials, indicate an increased risk of akathisia associated with the use of paroxetine. This is most likely to occur within the first few weeks of treatment.

Considering the above the CHMP concluded that a warning should be included in section 4.4 (Special Warnings and Special Precautions for Use) of the SPC to reflect the risk of development of akathisia in patients treated with paroxetine.

Long-term safety in children

The CHMP noted that long-term safety data in children and adolescents concerning growth, maturation and cognitive and behavioural development are lacking.

OVERALL CONCLUSION ON BENEFIT/RISK

Regarding efficacy, the CHMP concluded that paroxetine is effective in the treatment of major depressive episode, obsessive compulsive disorder, panic disorder with and without agarophobia, social anxiety disorder/social phobia, generalised anxiety disorder and post-traumatic stress disorder in adults. The CHMP also concluded that efficacy has not been demonstrated in children and adolescents with major depressive disorder. Insufficient evidence has been made available concerning the efficacy of paroxetine in this population for the treatment of obsessive compulsive disorder and social anxiety/social phobia. No studies are available in children and adolescents in the other currently approved indications for adults.

Regarding safety, data from clinical trials show that paroxetine is associated with an increased risk of suicidal and hostility related behaviours in the paediatric population (7-17 years old). Based on data from clinical trials and from post marketing there is a possibility of an increased risk of suicidal related behaviour associated with paroxetine in young adults (18-29 years). Paroxetine is associated with

withdrawal reactions which can be severe in intensity and prolonged in duration. Paroxetine use has been associated with the development of akathisia.

Therefore the CHMP considered that the benefit/risk balance of paroxetine containing medicinal products in the agreed indications is favourable and the Marketing Authorisations should be maintained in accordance with the:

1. Summary of Product Characteristics set out in Annex III of the CHMP Opinion with emphasis to the following:

- Therapeutic Indications

Treatment of

- Major Depressive Episode
- Obsessive Compulsive Disorder
- Panic Disorder with and without agoraphobia
- Social Anxiety Disorders/Social phobia
- Generalised Anxiety Disorder
- Post-traumatic Stress Disorder

- Posology and Method of Administration

Review of the wording with regards to the possibility of increasing the recommended dose if after some weeks of treatment on the recommended dose insufficient response is seen.
Strengthening of warnings concerning withdrawal symptoms seen on discontinuation of paroxetine and the need for down titration.
Inclusion of information concerning the lack of efficacy and increased risk of suicidal and hostility related behaviours in children and adolescents (7-17).

- Special Warnings and Special Precautions for Use

Inclusion/reinforcement of warnings concerning the lack of efficacy and increased risk of suicidal and hostility related behaviours in children and adolescents (7-17), suicide/suicidal ideation and withdrawal symptoms.

- Pregnancy and Lactation

Inclusion of information on the symptoms which can occur in the neonate after maternal paroxetine use in later stages of pregnancy.

- Undesirable effects

Expansion of withdrawal symptoms seen on discontinuation of paroxetine treatment and inclusion of information on adverse events from paediatric clinical trials.

- Pharmacodynamic Properties

Inclusion of information concerning long-term efficacy of paroxetine and dose response studies.

2. Conditions set out in Annex IV of the CHMP Opinion, including the submission of 6-monthly Periodic Safety Update Reports for the next two years.

The CHMP, having considered the additional data that became available after the opinion of 22 April 2004, concluded that such data do not change its previous conclusions and recommendations.

GROUNDS FOR AMENDMENT OF THE SUMMARIES OF PRODUCT CHARACTERISTICS

Whereas

- The Committee considered the referral made under article 31 of Directive 2001/83/EC, as amended, for paroxetine containing medicinal products.

- The Committee considered that paroxetine containing medicinal products are effective in the treatment of major depressive episode, obsessive compulsive disorder, panic disorder with and without agarophobia, social anxiety disorder/social phobia, generalised anxiety disorder and post-traumatic stress disorder in adults.

- The Committee considered that efficacy has not been demonstrated in children and adolescents with major depressive disorder. Insufficient evidence has been made available concerning the efficacy of paroxetine in this population for the treatment of obsessive compulsive disorder and social anxiety/social phobia. No studies are available in children and adolescents in the other currently approved indications for adults.

- The Committee concluded that there are concerns in relation to the safety of paroxetine containing medicinal products. Paroxetine is associated with an increased risk of suicidal and hostility related behaviours in the paediatric population (7-17 years old), a possibility of an increased risk of suicidal related behaviours in young adults (18-29 years), is also associated with withdrawal reactions which can be severe in intensity and prolonged in duration and with the development of akathisia.

- The Committee, as a consequence, considered the benefit/risk balance of paroxetine containing medicinal products to be favourable in the treatment of major depressive episode, obsessive compulsive disorder, panic disorder with and without agarophobia, social anxiety disorder/social phobia, generalised anxiety disorder and post-traumatic stress disorder in adults.

As a consequence, the CHMP has recommended the maintenance of the Marketing Authorisations for paroxetine containing medicinal products referred in Annex I as amended in accordance with the SPC set out in Annex III and under the conditions set out in Annex IV.

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS

Note: This Summary of Product Characteristics (SPC) is the one that was Annexed to the Commission Decision on this Article 31 referral for paroxetine containing medicinal products. The text was valid at that time.

After the Commission Decision, the Member State competent authorities will update the product information as required. Therefore, this SPC may not necessarily represent the current text.

1. NAME OF MEDICINAL PRODUCT

{*INVENTED NAME*} {Strength} {Pharmaceutical form}

[To be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

<Each <tablet><coated tablet><film-coated tablet> contains <10 mg><20 mg><30 mg><40 mg> paroxetine
<Each ml of <oral solution><oral suspension> contains <2 mg> paroxetine

[To be completed nationally]

3. PHARMACEUTICAL FORM

<Tablet> <Coated tablet> <Film-coated tablet>
<Oral solution> <Oral suspension>

[To be completed nationally]

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Treatment of
- Major Depressive Episode
- Obsessive Compulsive Disorder
- Panic Disorder with and without agoraphobia
- Social Anxiety Disorders/Social phobia
- Generalised Anxiety Disorder
- Post-traumatic Stress Disorder

4.2 Posology and Method of Administration

It is recommended that paroxetine is administered once daily in the morning with food.
<The tablet should be swallowed rather than chewed.>
<Shake bottle before use.>

[To be completed nationally]

MAJOR DEPRESSIVE EPISODE

The recommended dose is 20 mg daily. In general, improvement in patients starts after one week but may only become evident from the second week of therapy.
As with all antidepressant medicinal products, dosage should be reviewed and adjusted if necessary within 3 to 4 weeks of initiation of therapy and thereafter as judged clinically appropriate. In some patients, with insufficient response to 20 mg, the dose may be increased gradually up to a maximum of 50 mg a day in 10 mg steps according to the patient's response.

Patients with depression should be treated for a sufficient period of at least 6 months to ensure that they are free from symptoms.

OBSESSIVE COMPULSIVE DISORDER

The recommended dose is 40 mg daily. Patients should start on 20 mg/day and the dose may be increased gradually in 10 mg increments to the recommended dose. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually up to a maximum of 60 mg/day.
Patients with OCD should be treated for a sufficient period to ensure that they are free from symptoms. This period may be several months or even longer. (see section 5.1 Pharmacodynamic Properties)

PANIC DISORDER

The recommended dose is 40 mg daily. Patients should be started on 10 mg/day and the dose gradually increased in 10 mg steps according to the patient's response up to the recommended dose. A low initial starting dose is recommended to minimise the potential worsening of panic symptomatology, which is generally recognised to occur early in the treatment of this disorder. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually up to a maximum of 60 mg/day.
Patients with panic disorder should be treated for a sufficient period to ensure that they are free from symptoms. This period may be several months or even longer (see section 5.1 Pharmacodynamic Properties)

SOCIAL ANXIETY DISORDER/SOCIAL PHOBIA

The recommended dose is 20 mg daily. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually in 10 mg steps up to a maximum of 50 mg/day. Long-term use should be regularly evaluated (see section 5.1 Pharmacodynamic Properties).

GENERALISED ANXIETY DISORDER

The recommended dose is 20 mg daily. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually in 10 mg steps up to a maximum of 50 mg/day. Long-term use should be regularly evaluated (see section 5.1 Pharmacodynamic Properties).

POST-TRAUMATIC STRESS DISORDER

The recommended dose is 20 mg daily. If after some weeks on the recommended dose insufficient response is seen some patients may benefit from having their dose increased gradually in 10 mg steps up to a maximum of 50 mg/day. Long-term use should be regularly evaluated (see section 5.1 Pharmacodynamic Properties).

GENERAL INFORMATION

WITHDRAWAL SYMPTOMS SEEN ON DISCONTINUATION OF PAROXETINE
Abrupt discontinuation should be avoided (see section 4.4 Special Warnings and Special Precautions for Use and section 4.8 Undesirable Effects). The taper phase regimen used in clinical trials involved decreasing the daily dose by 10 mg at weekly intervals. If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the physician may continue decreasing the dose, but at a more gradual rate.

Special Populations:

- **Elderly**

Increased plasma concentrations of paroxetine occur in elderly subjects, but the range of concentrations overlaps with that observed in younger subjects. Dosing should commence at the adult starting dose. Increasing the dose might be useful in some patients, but the maximum dose should not exceed 40 mg daily.

- **Children and adolescents (7-17 years)**

Paroxetine should not be used for the treatment of children and adolescents as controlled clinical trials have found paroxetine to be associated with increased risk for suicidal behaviour and hostility. In addition, in these trials efficacy has not been adequately demonstrated (see section 4.4 Special Warnings and Special Precautions for use and section 4.8 Undesirable Effects).

- **Children aged below 7 years**

The use of paroxetine has not been studied in children less than 7 years. Paroxetine should not be used, as long as safety and efficacy in this age group have not been established.

- **Renal/hepatic impairment**

Increased plasma concentrations of paroxetine occur in patients with severe renal impairment (creatinine clearance less than 30 ml/min) or in those with hepatic impairment. Therefore, dosage should be restricted to the lower end of the dosage range.

4.3 Contraindications

Known hypersensitivity to paroxetine or any of the excipients.

Paroxetine is contraindicated in combination with monoamine oxidase inhibitors (MAOIs). Treatment with paroxetine can be initiated:
- two weeks after discontinuation of an irreversible MAOI, or
- at least 24hrs after discontinuation of a reversible MAOI (e.g. moclobemide).

At least one week should elapse between discontinuation of paroxetine and initiation of therapy with any MAOI.

Paroxetine should not be used in combination with thioridazine, because, as with other drugs which inhibit the hepatic enzyme CYP450 2D6, paroxetine can elevate plasma levels of thioridazine (see section 4.5 Interactions with other medicinal products and other forms of interaction). Administration of thioridazine alone can lead to QTc interval prolongation with associated serious ventricular arrhythmia such as torsades de pointes, and sudden death.

4.4 Special Warnings and Special Precautions for use

Treatment with paroxetine should be initiated cautiously two weeks after terminating treatment with an irreversible MAOI or 24 hours after terminating treatment with a reversible MAO inhibitor. Dosage of paroxetine should be increased gradually until an optimal response is reached (see section 4.3 Contraindications and section 4.5 Interactions with other medicinal products and other forms of interaction).

Children and Adolescents (7-17 years)

Paroxetine should not be used in the treatment of children and adolescents under the age of 18 years. In clinical trials increased suicidal related behaviours (suicide attempts and suicidal thoughts) and hostility (predominantly aggression, oppositional behaviour and anger) were more frequently observed in children and adolescents treated with paroxetine compared to those treated with placebo. In addition, in these trials efficacy has not been adequately demonstrated and long-term safety data in

children and adolescents concerning growth, maturation and cognitive and behavioural development are lacking (see section 4.8 Undesirable Effects).

Suicide/suicidal ideation
Depression is associated with an increased risk of suicidal thoughts, self harm and suicide. This risk persists until significant remission occurs. As improvement may not occur during the first few weeks or more of treatment, patients should be closely monitored until such improvement occurs. It is general clinical experience with all antidepressant therapies that the risk of suicide may increase in the early stages of recovery.

Other psychiatric conditions for which paroxetine is prescribed can also be associated with an increased risk of suicidal behaviour. In addition, these conditions may be co-morbid with major depressive disorder. The same precautions observed when treating patients with major depressive disorder should therefore be observed when treating patients with other psychiatric disorders.

Patients with a history of suicidal behaviour or thoughts, or those exhibiting a significant degree of suicidal ideation prior to commencement of treatment, are at a greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment.

There is a possibility of an increased risk of suicide related behaviour in young adults ages 18-29. Young adults should therefore be monitored carefully throughout treatment.

There are insufficient data concerning the risk of suicide related behaviour in treatment naïve patients, but careful monitoring might be warranted.

Patients, (and caregivers of patients) should be alerted about the need to monitor for the emergence of suicidal ideation/behaviour or thoughts of harming themselves and to seek medical advice immediately if these symptoms present.

Akathisia
The use of paroxetine has been associated with the development of akathisia, which is characterized by an inner sense of restlessness and psychomotor agitation such as an inability to sit or stand still usually associated with subjective distress. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

Serotonin Syndrome/Neuroleptic Malignant Syndrome
On rare occasions development of a serotonin syndrome or neuroleptic malignant syndrome-like events may occur in association with treatment of paroxetine, particularly when given in combination with other serotonergic and/or neuroleptic drugs. As these syndromes may result in potentially life-threatening conditions, treatment with paroxetine should be discontinued if such events (characterised by clusters of symptoms such as hyperthermia, rigidity, myoclonus, autonomic instability with possible rapid fluctuations of vital signs, mental status changes including confusion, irritability, extreme agitation progressing to delirium and coma) occur and supportive symptomatic treatment should be initiated. Paroxetine should not be used in combination with serotonin-precursors (such as L-tryptophan, oxitriptan) due to the risk of serotonergic syndrome.
(See Sections 4.3 Contraindications and 4.5 Interactions with other medicinal products and other forms of interaction).

Mania
As with all antidepressants, paroxetine should be used with caution in patients with a history of mania. Paroxetine should be discontinued in any patient entering a manic phase.

Renal/hepatic impairment
Caution is recommended in patients with severe renal impairment or in those with hepatic impairment. (see section 4.2 Posology and Method of Administration)

Diabetes
In patients with diabetes, treatment with an SSRI may alter glycaemic control. Insulin and/or oral hypoglycaemic dosage may need to be adjusted.

Epilepsy
As with other antidepressants, paroxetine should be used with caution in patients with epilepsy.

Seizures
Overall the incidence of seizures is less than 0.1% in patients treated with paroxetine. The drug should be discontinued in any patient who develops seizures.

ECT
There is little clinical experience of the concurrent administration of paroxetine with ECT.

Glaucoma
As with other SSRI's, paroxetine infrequently causes mydriasis and should be used with caution in patients with narrow angle glaucoma or history of glaucoma.

Cardiac Conditions
The usual precautions should be observed in patients with cardiac conditions.

Hyponatraemia
Hyponatraemia has been reported rarely, predominantly in the elderly. Caution should also be exercised in those patients at risk of hyponatraemia e.g. from concomitant medications and cirrhosis. The hyponatraemia generally reverses on discontinuation of paroxetine.

Haemorrhage
There have been reports of cutaneous bleeding abnormalities such as ecchymoses and purpura with SSRIs. Other haemorrhagic manifestations e.g. gastrointestinal haemorrhage have been reported. Elderly patients may be at an increased risk.

Caution is advised in patients taking SSRI's concomitantly with oral anticoagulants, drugs known to affect platelet function or other drugs that may increase risk of bleeding (e.g. atypical antipsychotics such as clozapine, phenothiazines, most TCA's, acetylsalicylic acid, NSAID's, COX-2 inhibitors) as well as in patients with a history of bleeding disorders or conditions which may predispose to bleeding.

<Parabens>
<Paroxetine oral suspension contains methyl and propyl hydroxybenzoate (parabens), which are known to cause urticaria; generally delayed type reactions, such as contact dermatitis, but rarely immediate reaction with bronchospasm.> [To be completed nationally].

Withdrawal symptoms seen on discontinuation of paroxetine treatment

Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt (see section 4.8 Undesirable effects). In clinical trials adverse events seen on treatment discontinuation occurred in 30% of patients treated with paroxetine compared to 20% of patients treated with placebo. The occurrence of withdrawal symptoms is not the same as the drug being addictive or dependence producing.
The risk of withdrawal symptoms may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction.
Dizziness, sensory disturbances (including paraesthesia and electric shock sensations), sleep disturbances (including intense dreams), agitation or anxiety, nausea, tremor, confusion, sweating, headache, diarrhoea, palpitations, emotional instability, irritability, and visual disturbances have been reported. Generally these symptoms are mild to moderate, however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose.

Generally these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that paroxetine should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient's needs (see "Withdrawal Symptoms Seen on Discontinuation of Paroxetine", Section 4.2 Posology and Method of Administration).

4.5 Interactions with other medicinal products and other forms of interaction

Serotonergic drugs
As with other SSRIs, co-administration with serotonergic drugs (including MAOIs, L-tryptophan, triptans, tramadol, linezolid, SSRIs, lithium and St. John's Wort – Hypericum perforatum – preparations) may lead to an incidence of 5-HT associated effects (serotonin syndrome: see Section 4.3 Contraindications and Section 4.4 Special Warnings and Special Precautions for Use).
Caution should be advised and a closer clinical monitoring is required when these drugs are combined with paroxetine.

Drug metabolising enzymes
The metabolism and pharmacokinetics of paroxetine may be affected by the induction or inhibition of drug metabolising enzymes.
When paroxetine is to be co-administered with a known drug metabolising enzyme inhibitor, consideration should be given to using paroxetine doses at the lower end of the range.
No initial dosage adjustment is considered necessary when the drug is to be co-administered with known drug metabolising enzyme inducers (e.g. carbamazepine, rifampicin, phenobarbital, phenytoin). Any subsequent dosage adjustment should be guided by clinical effect (tolerability and efficacy).

Procyclidine: Daily administration of paroxetine increases significantly the plasma levels of procyclidine. If anti-cholinergic effects are seen, the dose of procyclidine should be reduced.

Anticonvulsants: carbamazepine, phenytoin, sodium valproate. Concomitant administration does not seem to show any effect on pharmacokinetic/dynamic profile in epileptic patients.

CYP2D6 inhibitory potency of paroxetine
As with other antidepressants, including other SSRIs, paroxetine inhibits the hepatic cytochrome P450 enzyme CYP2D6. Inhibition of CYP2D6 may lead to increased plasma concentrations of co-administered drugs metabolised by this enzyme. These include certain tricyclic antidepressants (e.g. clomipramine, nortriptyline, and desipramine), phenothiazine neuroleptics (e.g. perphenazine and thioridazine, see section 4.3 Contraindications), risperidone, certain Type 1c antiarrhythmics (e.g. propafenone and flecainide) and metoprolol. It is not recommended to use paroxetine in combination with metoprolol when given in cardiac insufficiency, because of the narrow therapeutic index of metoprolol in this indication.

Alcohol
As with other psychotropic drugs patients should be advised to avoid alcohol use while taking paroxetine.

Oral anticoagulants
A pharmacodynamic interaction between paroxetine and oral anticoagulants may occur. Concomitant use of paroxetine and oral anticoagulants can lead to an increased anticoagulant activity and haemorrhagic risk. Therefore, paroxetine should be used with caution in patients who are treated with oral anticoagulants. (see section 4.4 Special Warnings and Special Precautions for use**)**

NSAIDs and acetylsalicylic acid, and other antiplatelet agents
A pharmacodynamic interaction between paroxetine and NSAIDs/acetylsalicylic acid may occur. Concomitant use of paroxetine and NSAIDs/acetylsalicylic acid can lead to an increased haemorrhagic risk. (see section 4.4 Special warnings and Special Precautions for use)
Caution is advised in patients taking SSRI's, concomitantly with oral anticoagulants, drugs known to affect platelet function or increase risk of bleeding (e.g. atypical antipsychotics such as clozapine, phenothiazines, most TCA's, acetylsalicylic acid, NSAID's, COX-2 inhibitors) as well as in patients with a history of bleeding disorders or conditions which may predispose to bleeding.

4.6 Pregnancy and Lactation

Pregnancy
Data on a limited number of exposed pregnancies provide no indication of an increased risk of congenital malformations in the newborn.

Paroxetine should only be used during pregnancy when strictly indicated. Women planning a pregnancy and those becoming pregnant during therapy should be asked to consult their physician. Abrupt discontinuation should be avoided during pregnancy (see "Withdrawal Symptoms Seen on Discontinuation of Paroxetine", section 4.2 Posology and Method of Administration).

Neonates should be observed if maternal use of paroxetine continues into the later stages of pregnancy, particularly the third trimester.

The following symptoms may occur in the neonate after maternal paroxetine use in later stages of pregnancy: respiratory distress, cyanosis, apnoea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycaemia, hypertonia, hypotonia, hyperreflexia, tremor, jitteriness, irritability, lethargy, constant crying, somnolence and difficulty in sleeping . These symptoms could be due to either serotonergic effects or withdrawal symptoms. In a majority of instances the complications begin immediately or soon (<24 hours) after delivery.

Animal studies showed reproductive toxicity, but did not indicate direct harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development (see Section 5.3 Preclinical Safety Data).

Lactation
Small amounts of paroxetine are excreted into breast milk. In published studies, serum concentrations in breast-fed infants were undetectable (<2 ng/ml) or very low (<4 ng/ml). No signs of drug effects were observed in these infants. Nevertheless, paroxetine should not be used during lactation unless the expected benefits to the mother justify the potential risks for the infant.

4.7 Effects on Ability to Drive and Use Machines

Clinical experience has shown that therapy with paroxetine is not associated with impairment of cognitive or psychomotor function. However, as with all psychoactive drugs, patients should be cautioned about their ability to drive a car and operate machinery.
Although paroxetine does not increase the mental and motor skill impairments caused by alcohol, the concomitant use of paroxetine and alcohol is not advised.

4.8 Undesirable Effects

Some of the adverse drug reactions listed below may decrease in intensity and frequency with continued treatment and do not generally lead to cessation of therapy. Adverse drug reactions are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), common (≥ 1/100, <1/10), uncommon (≥ 1/1,000, <1/100), rare (≥ 1/10,000, <1/1,000), very rare (<1/10,000), including isolated reports.

Blood and lymphatic system disorders
Uncommon: abnormal bleeding, predominantly of the skin and mucous membranes (mostly ecchymosis).
Very rare: thrombocytopenia.

Immune system disorders
Very rare: allergic reactions (including urticaria and angioedema).

Endocrine disorders
Very rare: syndrome of inappropriate anti-diuretic hormone secretion (SIADH).

Metabolism and nutrition disorders
Common: decreased appetite.
Rare: hyponatraemia.
Hyponatraemia has been reported predominantly in elderly patients and is sometimes due to syndrome of inappropriate anti-diuretic hormone secretion (SIADH).

Psychiatric disorders
Common: somnolence, insomnia.
Uncommon: confusion, hallucinations.
Rare: manic reactions, agitation, anxiety, depersonalisation, panic attacks, akathisia (see section 4.4 Special Warnings and Special Precautions for use).
These symptoms may also be due to the underlying disease

Nervous system disorders
Common: dizziness, tremor
Uncommon: extrapyramidal disorders
Rare: convulsions.
Very rare: serotonin syndrome (symptoms may include agitation, confusion, diaphoresis, hallucinations, hyperreflexia, myoclonus, shivering, tachycardia and tremor).
Reports of extrapyramidal disorder including oro-facial dystonia have been received in patients sometimes with underlying movement disorders or who were using neuroleptic medication.

Eye disorders
Common: blurred vision.
Very rare: acute glaucoma.

Cardiac disorders
Uncommon: sinus tachycardia.
Rare: bradycardia.

Vascular disorders
Uncommon: transient increases or decreases in blood pressure.
Transient increases or decreases of blood pressure have been reported following treatment with paroxetine, usually in patients with pre-existing hypertension or anxiety.

Respiratory, thoracic and mediastinal disorders
Common: yawning.

Gastrointestinal disorders
Very common: nausea.
Common: constipation, diarrhoea, dry mouth.
Very rare: gastrointestinal bleeding.

Hepato-biliary disorders
Rare: elevation of hepatic enzymes.
Very rare: hepatic events (such as hepatitis, sometimes associated with jaundice and/or liver failure).

Elevation of hepatic enzymes have been reported. Post-marketing reports of hepatic events (such as hepatitis, sometimes associated with jaundice and/or liver failure) have also been received very rarely. Discontinuation of paroxetine should be considered if there is prolonged elevation of liver function test results.

Skin and subcutaneous tissue disorders
Common: sweating.
Uncommon: skin rashes, pruritus
Very rare: photosensitivity reactions.

Renal and urinary disorders
Uncommon: urinary retention.

Reproductive system and breast disorders
Very common: sexual dysfunction.
Rare: hyperprolactinaemia/galactorrhoea.
Very rare: priapism.

Musculoskeletal disorders
Rare: arthralgia, myalgia

General disorder and administration site conditions
Common: asthenia, body weight gain
Very rare: peripheral oedema.

WITHDRAWAL SYMPTOMS SEEN ON DISCONTINUATION OF PAROXETINE TREATMENT

Common: dizziness, sensory disturbances, sleep disturbances, anxiety, headache.
Uncommon: agitation, nausea, tremor, confusion, sweating, emotional instability, visual disturbances, palpitations, diarrhoea, irritability.
Discontinuation of paroxetine (particularly when abrupt) commonly leads to withdrawal symptoms. Dizziness, sensory disturbances (including paraesthesia and electric shock sensations), sleep disturbances (including intense dreams), agitation or anxiety, nausea, tremor, confusion, sweating, headache, diarrhoea, palpitations, emotional instability, irritability, and visual disturbances have been reported.
Generally these events are mild to moderate and are self-limiting, however, in some patients they may be severe and/or prolonged. It is therefore advised that when paroxetine treatment is no longer required, gradual discontinuation by dose tapering should be carried out (see section 4.2 Posology and Method of Administration and section 4.4 Special Warnings and Special Precautions for use).

ADVERSE EVENTS FROM PAEDIATRIC CLINICAL TRIALS
In short-term (up to 10-12 weeks) clinical trials in children and adolescents, the following adverse events were observed in paroxetine treated patients at a frequency of at least 2% of patients and occurred at a rate at least twice that of placebo were: increased suicidal related behaviours (including suicide attempts and suicidal thoughts), self-harm behaviours and increased hostility. Suicidal thoughts and suicide attempts were mainly observed in clinical trials of adolescents with Major Depressive Disorder. Increased hostility occurred particularly in children with obsessive compulsive disorder, and especially in younger children less than 12 years of age. Additional events that were more often seen in the paroxetine compared to placebo group were: decreased appetite, tremor, sweating, hyperkinesia, agitation, emotional lability (including crying and mood fluctuations).

In studies that used a tapering regimen, symptoms reported during the taper phase or upon discontinuation of paroxetine at a frequency of at least 2% of patients and occurred at a rate at least twice that of placebo were: emotional lability (including crying, mood fluctuations, self-harm, suicidal thoughts and attempted suicide), nervousness, dizziness, nausea and abdominal pain (see section 4.4 Special Warnings and Special Precautions for use).

4.9 Overdose

Symptoms and Signs
A wide margin of safety is evident from available overdose information on paroxetine.
Experience of paroxetine in overdose has indicated that, in addition to those symptoms mentioned under section 4.8 "Undesirable Effects", vomiting, dilated pupils, fever, blood pressure changes, headache, involuntary muscle contractions, agitation, anxiety and tachycardia have been reported. Patients have generally recovered without serious sequelae even when doses of up to 2000 mg have been taken alone. Events such as coma or ECG changes have occasionally been reported and, very rarely with a fatal outcome, but generally when paroxetine was taken in conjunction with other psychotropic drugs, with or without alcohol.

Treatment
No specific antidote is known.
The treatment should consist of those general measures employed in the management of overdose with any antidepressant. Where appropriate, the stomach should be emptied either by the induction of emesis, lavage or both. Following evacuation, 20 to 30 g of activated charcoal may be administered every 4 to 6 h during the first 24 h after ingestion. Supportive care with frequent monitoring of vital signs and careful observation is indicated.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group: Antidepressants – selective serotonin reuptake inhibitors, ATC code: N06A B05

Mechanism of Action
Paroxetine is a potent and selective inhibitor of 5-hydroxytryptamine (5-HT, serotonin) uptake and its antidepressant action and effectiveness in the treatment of OCD, Social Anxiety disorder/Social Phobia, General Anxiety Disorder, Post-traumatic Stress Disorder and Panic Disorder is thought to be related to its specific inhibition of 5-HT uptake in brain neurones.
Paroxetine is chemically unrelated to the tricyclic, tetracyclic and other available antidepressants. Paroxetine has low affinity for muscarinic cholinergic receptors and animal studies have indicated only weak anticholinergic properties.
In accordance with this selective action, *in vitro* studies have indicated that, in contrast to tricyclic antidepressants, paroxetine has little affinity for alpha1, alpha2 and beta-adrenoceptors, dopamine (D2), 5-HT1 like, 5-HT2 and histamine (H1) receptors. This lack of interaction with post-synaptic receptors *in vitro* is substantiated by *in vivo* studies which demonstrate lack of CNS depressant and hypotensive properties.

Pharmacodynamic Effects
Paroxetine does not impair psychomotor function and does not potentiate the depressant effects of ethanol.
As with other selective 5-HT uptake inhibitors, paroxetine causes symptoms of excessive 5-HT receptor stimulation when administered to animals previously given monoamine oxidase (MAO) inhibitors or tryptophan.
Behavioural and EEG studies indicate that paroxetine is weakly activating at doses generally above those required to inhibit 5-HT uptake. The activating properties are not "amphetamine-like" in nature.
Animal studies indicate that paroxetine is well tolerated by the cardiovascular system. Paroxetine produces no clinically significant changes in blood pressure, heart rate and ECG after administration to healthy subjects.
Studies indicate that, in contrast to antidepressants which inhibit the uptake of noradrenaline, paroxetine has a much reduced propensity to inhibit the antihypertensive effects of guanethidine.

In the treatment of depressive disorders, paroxetine exhibits comparable efficacy to standard antidepressants.
There is also some evidence that paroxetine may be of therapeutic value in patients who have failed to respond to standard therapy.
Morning dosing with paroxetine does not have any detrimental effect on either the quality or duration of sleep. Moreover, patients are likely to experience improved sleep as they respond to paroxetine therapy.

Dose response
In the fixed dose studies there is a flat dose response curve, providing no suggestion of advantage in terms of efficacy for using higher than the recommended doses. However, there are some clinical data suggesting that up-titrating the dose might be beneficial for some patients.

Long-term efficacy
The long-term efficacy of paroxetine in depression has been demonstrated in a 52 week maintenance study with relapse prevention design: 12% of patients receiving paroxetine (20-40mg daily) relapsed, versus 28% of patients on placebo.

The long-term efficacy of paroxetine in treating obsessive compulsive disorder has been examined in three 24 week maintenance studies with relapse prevention design. One of the three studies achieved a significant difference in the proportion of relapsers between paroxetine (38%) compared to placebo (59%).

The long-term efficacy of paroxetine in treating panic disorder has been demonstrated in a 24 week maintenance study with relapse prevention design: 5% of patients receiving paroxetine (10-40mg daily) relapsed, versus 30% of patients on placebo. This was supported by a 36 week maintenance study.

The long-term efficacy of paroxetine in treating social anxiety disorder and generalised anxiety disorder and Post-traumatic Stress Disorder has not been sufficiently demonstrated.

5.2 Pharmacokinetics

Absorption
Paroxetine is well absorbed after oral dosing and undergoes first-pass metabolism. Due to first-pass metabolism, the amount of paroxetine available to the systemic circulation is less than that absorbed from the gastrointestinal tract. Partial saturation of the first-pass effect and reduced plasma clearance occur as the body burden increases with higher single doses or on multiple dosing. This results in disproportionate increases in plasma concentrations of paroxetine and hence pharmacokinetic parameters are not constant, resulting in non-linear kinetics. However, the non-linearity is generally small and is confined to those subjects who achieve low plasma levels at low doses.
Steady state systemic levels are attained by 7 to 14 days after starting treatment with immediate or controlled release formulations and pharmacokinetics do not appear to change during long-term therapy.

Distribution
Paroxetine is extensively distributed into tissues and pharmacokinetic calculations indicate that only 1% of the paroxetine in the body resides in the plasma.
Approximately 95% of the paroxetine present is protein bound at therapeutic concentrations.
No correlation has been found between paroxetine plasma concentrations and clinical effect (adverse experiences and efficacy).
Transfer to human breast milk, and to the foetuses of laboratory animals, occurs in small amounts.

Metabolism
The principal metabolites of paroxetine are polar and conjugated products of oxidation and methylation which are readily cleared. In view of their relative lack of pharmacological activity, it is most unlikely that they contribute to paroxetine's therapeutic effects.

Metabolism does not compromise paroxetine's selective action on neuronal 5-HT uptake.

Elimination
Urinary excretion of unchanged paroxetine is generally less than 2% of dose whilst that of metabolites is about 64% of dose. About 36% of the dose is excreted in faeces, probably via the bile, of which unchanged paroxetine represents less than 1% of the dose. Thus paroxetine is eliminated almost entirely by metabolism.
Metabolite excretion is biphasic, being initially a result of first-pass metabolism and subsequently controlled by systemic elimination of paroxetine.
The elimination half-life is variable but is generally about 1 day.

Special Patient Populations

Elderly and Renal/Hepatic Impairment
Increased plasma concentrations of paroxetine occur in elderly subjects and in those subjects with severe renal impairment or in those with hepatic impairment, but the range of plasma concentrations overlaps that of healthy adult subjects.

5.3 Preclinical safety data

Toxicology studies have been conducted in rhesus monkeys and albino rats; in both, the metabolic pathway is similar to that described for humans. As expected with lipophilic amines, including tricyclic antidepressants, phospholipidosis was detected in rats. Phospholipidosis was not observed in primate studies of up to one-year duration at doses that were 6 times higher than the recommended range of clinical doses.
Carcinogenesis: In two-year studies conducted in mice and rats, paroxetine had no tumorigenic effect.
Genotoxicity: Genotoxicity was not observed in a battery of *in vitro* and *in vivo* tests.
Reproduction toxicity studies in rats have shown that paroxetine affects male and female fertility. In rats, increased pup mortality and delayed ossification were observed. The latter effects were likely related to maternal toxicity and are not considered a direct effect on the foetus/neonate.

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]

7. MARKETING AUTHORISATION HOLDER

[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

ANNEX IV

CONDITIONS OF THE MARKETING AUTHORISATION

Conditions of the Marketing Authorisations

- Member States should ensure that appropriate pharmaceutical forms / strengths can be made available in order to facilitate up and down titration in accordance to the posology recommendations stated in the SPC attached to Annex III of this Opinion.

- 6-monthly Periodic Safety Update Reports should be provided to the Reference Member States and/or National Competent Authorities for the next 2 years.

