ANNEX I

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

Member State	Marketing Authorisation Holder	(Invented) Name	Strength	Pharmaceutical form	Route of administration
Austria	GlaxoSmithKline Pharma GmbH, Albert-Schweitzer-Gasse 6 A-1140 Wien Austria	Lamictal 5mg - lösliche Tabletten	5 mg	Dispersible Tablet	Oral use
Austria	GlaxoSmithKline Pharma GmbH, Albert-Schweitzer-Gasse 6 A-1140 Wien Austria	Lamictal 25mg - lösliche Tabletten	25 mg	Dispersible Tablet	Oral use
Austria	GlaxoSmithKline Pharma GmbH, Albert-Schweitzer-Gasse 6 A-1140 Wien Austria	Lamictal 50mg - lösliche Tabletten	50 mg	Dispersible Tablet	Oral use
Austria	GlaxoSmithKline Pharma GmbH, Albert-Schweitzer-Gasse 6 A-1140 Wien Austria	Lamictal 100mg - lösliche Tabletten	100 mg	Dispersible Tablet	Oral use
Austria	GlaxoSmithKline Pharma GmbH, Albert-Schweitzer-Gasse 6 A-1140 Wien Austria	Lamictal 200mg - lösliche Tabletten	200 mg	Dispersible Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal	25 mg	Tablet	Oral use

Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal	50 mg	Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal	100 mg	Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal Dispersible 25mg Starter-Pack Mono	25 mg	Dispersible Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal Dispersible 25mg Starter-Pack Add-on	25 mg	Dispersible Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal Dispersible 50mg Starter-Pack add-on	50 mg	Dispersible Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	2 mg	Dispersible Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	5 mg	Dispersible Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	25 mg	Dispersible Tablet	Oral use

Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	50 mg	Dispersible Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	100 mg	Dispersible Tablet	Oral use
Belgium	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	200 mg	Dispersible Tablet	Oral use
Bulgaria	GlaxoSmithKline EOOD, Ivan Vazov complex Dimitar Manov street, bl.10, Sofia 1408 Bulgaria	Lamictal	25 mg	Tablet	Oral use
Bulgaria	GlaxoSmithKline EOOD, Ivan Vazov complex Dimitar Manov street, bl.10, Sofia 1408 Bulgaria	Lamictal	50 mg	Tablet	Oral use
Bulgaria	GlaxoSmithKline EOOD, Ivan Vazov complex Dimitar Manov street, bl.10, Sofia 1408 Bulgaria	Lamictal	100 mg	Tablet	Oral use
Bulgaria	Glaxo Group Ltd Greenford Road Greenford Middlesex UB6 0NN United Kingdom	Lamictal	5 mg	Dispersible Tablet	Oral use

Cyprus	Glaxo Group Ltd Berkeley Avenue Greenford Middlesex UB6 0NN United Kingdom	Lamictal	5 mg	Dispersible Tablet	Oral use
Cyprus	Glaxo Group Ltd Berkeley Avenue Greenford Middlesex UB6 0NN United Kingdom	Lamictal	25mg	Dispersible Tablet	Oral use
Cyprus	Glaxo Group Ltd Berkeley Avenue Greenford Middlesex UB6 0NN United Kingdom	Lamictal	50 mg	Dispersible Tablet	Oral use
Cyprus	Glaxo Group Ltd Berkeley Avenue Greenford Middlesex UB6 0NN United Kingdom	Lamictal	100 mg	Dispersible Tablet	Oral use
Cyprus	Glaxo Group Ltd Berkeley Avenue Greenford Middlesex UB6 0NN United Kingdom	Lamictal	200 mg	Dispersible Tablet	Oral use

Czech Republic	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 25 mg	25 mg	Tablet	Oral use
Czech Republic	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 50 mg	50 mg	Tablet	Oral use
Czech Republic	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 100 mg	100 mg	Tablet	Oral use
Czech Republic	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 2 mg	2 mg	Dispersible Tablet	Oral use

Czech Republic	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 5 mg	5 mg	Dispersible Tablet	Oral use
Czech Republic	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 25 mg	25 mg	Dispersible Tablet	Oral use
Czech Republic	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 50 mg	50 mg	Dispersible Tablet	Oral use
Czech Republic	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 100 mg	100 mg	Dispersible Tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	25 mg	Tablet	Oral use

Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	50 mg	Tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	100 mg	Tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	200 mg	Tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	2 mg	Dispersible Tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	5 mg	Dispersible Tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	25 mg	Dispersible Tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	50 mg	Dispersible Tablet	Oral use
Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	100 mg	Dispersible Tablet	Oral use

Denmark	GlaxoSmithKline Pharma A/S Nykaer 68 DK-2605 Broendby Denmark	Lamictal	200 mg	Dispersible Tablet	Oral use
Estonia	Glaxo Wellcome Operations Greenford Road Greenford Middlesex UB6 0NN United Kingdom	Lamictal	2 mg	Dispersible Tablet	Oral use
Estonia	Glaxo Wellcome Operations Greenford Road Greenford Middlesex UB6 0NN United Kingdom	Lamictal	5 mg	Dispersible Tablet	Oral use
Estonia	Glaxo Wellcome Operations Greenford Road Greenford Middlesex UB6 0NN United Kingdom	Lamictal	25 mg	Dispersible Tablet	Oral use
Estonia	Glaxo Wellcome Operations Greenford Road Greenford Middlesex UB6 0NN United Kingdom	Lamictal	50 mg	Dispersible Tablet	Oral use
Estonia	Glaxo Wellcome Operations Greenford Road Greenford Middlesex UB6 0NN United Kingdom	Lamictal	100 mg	Dispersible Tablet	Oral use

Estonia	Glaxo Wellcome Operations Greenford Road Greenford Middlesex UB6 0NN United Kingdom	Lamictal	200 mg	Dispersible Tablet	Oral use
Finland	GlaxoSmithKline Oy Piispansilta 9 A 02230 Espoo Finland	Lamictal	2 mg	Dispersible Tablet	Oral use
Finland	GlaxoSmithKline Oy Piispansilta 9 A 02230 Espoo Finland	Lamictal	5 mg	Dispersible Tablet	Oral use
Finland	GlaxoSmithKline Oy Piispansilta 9 A 02230 Espoo Finland	Lamictal	25 mg	Dispersible Tablet	Oral use
Finland	GlaxoSmithKline Oy Piispansilta 9 A 02230 Espoo Finland	Lamictal	50 mg	Dispersible Tablet	Oral use
Finland	GlaxoSmithKline Oy Piispansilta 9 A 02230 Espoo Finland	Lamictal	100 mg	Dispersible Tablet	Oral use
Finland	GlaxoSmithKline Oy Piispansilta 9 A 02230 Espoo Finland	Lamictal	200 mg	Dispersible Tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 Route de Versailles 78163 Marly-le-Roi Cedex France	Lamicstart 25 mg, comprimé	25 mg	Tablet	Oral use

France	Laboratoire GlaxoSmithKline 100 Route de Versailles 78163 Marly-le-Roi Cedex France	Lamicstart 50 mg, comprimé	50 mg	Tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 Route de Versailles 78163 Marly-le-Roi Cedex France	Lamictal 2 mg, comprimé dispersible	2 mg	Dispersible Tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 Route de Versailles 78163 Marly-le-Roi Cedex France	Lamictal 5 mg, comprimé dispersible ou à croquer	5 mg	Dispersible or chewable Tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 Route de Versailles 78163 Marly-le-Roi Cedex France	Lamictal 25 mg, comprimé dispersible ou à croquer	25 mg	Dispersible or chewable Tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 Route de Versailles 78163 Marly-le-Roi Cedex France	Lamictal 50 mg, comprimé dispersible ou à croquer	50 mg	Dispersible or chewable Tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 Route de Versailles 78163 Marly-le-Roi Cedex France	Lamictal 100 mg, comprimé dispersible ou à croquer	100 mg	Dispersible or chewable Tablet	Oral use
France	Laboratoire GlaxoSmithKline 100 Route de Versailles 78163 Marly-le-Roi Cedex France	Lamictal 200 mg, comprimé dispersible ou à croquer	200 mg	Dispersible or chewable Tablet	Oral use
Germany	GlaxoSmithKline GmbH & Co. KG Theresienhöhe 11 80339 München Germany	Lamictal 2 mg Tabletten zur Herstellung einer Suspension zum Einnehmen	2 mg	Dispersible Tablet	Oral use

Germany	GlaxoSmithKline GmbH & Co. KG Theresienhöhe 11 80339 München Germany	Lamictal 5 mg Tabletten zur Herstellung einer Suspension zum Einnehmen	5 mg	Dispersible Tablet	Oral use
Germany	GlaxoSmithKline GmbH & Co. KG Theresienhöhe 11 80339 München Germany	Lamictal 25 mg Tabletten zur Herstellung einer Suspension zum Einnehmen	25 mg	Dispersible Tablet	Oral use
Germany	GlaxoSmithKline GmbH & Co. KG Theresienhöhe 11 80339 München Germany	Lamictal 50 mg Tabletten zur Herstellung einer Suspension zum Einnehmen	50 mg	Dispersible Tablet	Oral use
Germany	GlaxoSmithKline GmbH & Co. KG Theresienhöhe 11 80339 München Germany	Lamictal 100 mg Tabletten zur Herstellung einer Suspension zum Einnehmen	100 mg	Dispersible Tablet	Oral use
Germany	GlaxoSmithKline GmbH & Co. KG Theresienhöhe 11 80339 München Germany	Lamictal 200 mg Tabletten zur Herstellung einer Suspension zum Einnehmen	200 mg	Dispersible Tablet	Oral use
Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	25 mg	Tablet	Oral use

Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	50 mg	Tablet	Oral use
Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	100 mg	Tablet	Oral use
Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	200 mg	Tablet	Oral use
Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	2 mg	Dispersible/Chewable Tablets	Oral use
Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	5 mg	Dispersible/Chewable Tablets	Oral use
Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	25 mg	Dispersible/Chewable Tablets	Oral use

Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	50 mg	Dispersible/Chewable Tablets	Oral use
Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	100 mg	Dispersible/Chewable Tablets	Oral use
Greece	GlaxoSmithKline α.ε.β.ε 266 Kifissias Ave 152 32 Halandri Athens Greece	Lamictal	200 mg	Dispersible/Chewable Tablets	Oral use
Hungary	GlaxoSmithKline Kft. 1124Bp. Csorsz u. 43. MOM Park, Gesztenyes torony Hungary	Lamictal	25 mg	Tablet	Oral use
Hungary	GlaxoSmithKline Kft. 1124Bp. Csorsz u. 43. MOM Park, Gesztenyes torony Hungary	Lamictal	50 mg	Tablet	Oral use
Hungary	GlaxoSmithKline Kft. 1124Bp. Csorsz u. 43. MOM Park, Gesztenyes torony Hungary	Lamictal	100 mg	Tablet	Oral use
Hungary	GlaxoSmithKline Kft. 1124Bp. Csorsz u. 43. MOM Park, Gesztenyes torony Hungary	Lamictal	5 mg	Dispersible Tablet	Oral use

Hungary	GlaxoSmithKline Kft. 1124Bp. Csorsz u. 43. MOM Park, Gesztenyes torony Hungary	Lamictal	200 mg	Dispersible Tablet	Oral use
Iceland	GlaxoSmithKline ehf. Thverholt 14 105 Reykjavik Iceland	Lamictal	2 mg	Dispersible Tablet	Oral use
Iceland	GlaxoSmithKline ehf. Thverholt 14 105 Reykjavik Iceland	Lamictal	5 mg	Dispersible Tablet	Oral use
Iceland	GlaxoSmithKline ehf. Thverholt 14 105 Reykjavik Iceland	Lamictal	25 mg	Dispersible Tablet	Oral use
Iceland	GlaxoSmithKline ehf. Thverholt 14 105 Reykjavik Iceland	Lamictal	50 mg	Dispersible Tablet	Oral use
Iceland	GlaxoSmithKline ehf. Thverholt 14 105 Reykjavik Iceland	Lamictal	100 mg	Dispersible Tablet	Oral use
Iceland	GlaxoSmithKline ehf. Thverholt 14 105 Reykjavik Iceland	Lamictal	200 mg	Dispersible Tablet	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal Tablets 25mg	25 mg	Tablet	Oral use

Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal Tablets 50mg	50 mg	Tablet	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal Tablets 100mg	100 mg	Tablet	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal Tablets 200mg	200 mg	Tablet	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal 2mg Dispersible Tablets	2 mg	Dispersible Tablet	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal Dispersible Tablets 5mg	5 mg	Dispersible Tablet	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal Dispersible Tablets 25mg	25 mg	Dispersible Tablet	Oral use

Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal Dispersible Tablets 50mg	50 mg	Dispersible Tablet	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal Dispersible Tablets 100mg	100 mg	Dispersible Tablet	Oral use
Ireland	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal Dispersible Tablets 200mg	200 mg	Dispersible Tablet	Oral use
Italy	GlaxoSmithKline SpA Via Fleming 2 37135 Verona Italy	Lamictal	5 mg	Dispersible Tablet	Oral use
Italy	GlaxoSmithKline SpA Via Fleming 2 37135 Verona Italy	Lamictal	25 mg	Dispersible Tablet	Oral use
Italy	GlaxoSmithKline SpA Via Fleming 2 37135 Verona Italy	Lamictal	50 mg	Dispersible Tablet	Oral use
Italy	GlaxoSmithKline SpA Via Fleming 2 37135 Verona Italy	Lamictal	100 mg	Dispersible Tablet	Oral use

Italy	GlaxoSmithKline SpA Via Fleming 2 37135 Verona Italy	Lamictal	200 mg	Dispersible Tablet	Oral use
Latvia	GlaxoSmithKline Latvia SIA Bruninieku iela 5 Riga LV-1001 Latvia	Lamictal 2 mg dispersible tablets	2 mg	Dispersible Tablet	Oral use
Latvia	GlaxoSmithKline Latvia SIA Bruninieku iela 5 Riga LV-1001 Latvia	Lamictal 5 mg dispersible tablets	5 mg	Dispersible Tablet	Oral use
Latvia	GlaxoSmithKline Latvia SIA Bruninieku iela 5 Riga LV-1001 Latvia	Lamictal 25 mg dispersible tablets	25 mg	Dispersible Tablet	Oral use
Latvia	GlaxoSmithKline Latvia SIA Bruninieku iela 5 Riga LV-1001 Latvia	Lamictal 50 mg dispersible tablets	50 mg	Dispersible Tablet	Oral use
Latvia	GlaxoSmithKline Latvia SIA Bruninieku iela 5 Riga LV-1001 Latvia	Lamictal 100 mg dispersible tablets	100 mg	Dispersible Tablet	Oral use
Latvia	GlaxoSmithKline Latvia SIA Bruninieku iela 5 Riga LV-1001 Latvia	Lamictal 200 mg dispersible tablets	200 mg	Dispersible Tablet	Oral use

Lithuania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal	5 mg	Dispersible Tablet	Oral use
Lithuania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal	25 mg	Dispersible Tablet	Oral use
Lithuania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal	50 mg	Dispersible Tablet	Oral use
Lithuania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal	100 mg	Dispersible Tablet	Oral use

Lithuania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal	200 mg	Dispersible Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal	25 mg	Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal	50 mg	Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal	100 mg	Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal Dispersible 25mg Starter-Pack Mono	25 mg	Dispersible Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal Dispersible 25mg Starter-Pack Add-on	25 mg	Dispersible Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal Dispersible 50mg Starter-Pack add-on	50 mg	Dispersible Tablet	Oral use

Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	2 mg	Dispersible Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	5 mg	Dispersible Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	25 mg	Dispersible Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	50 mg	Dispersible Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	100 mg	Dispersible Tablet	Oral use
Luxembourg	GlaxoSmithKline s.a. Rue du Tilleul 13, B86 1332 Genval Belgium	Lamictal dispersible	200 mg	Dispersible Tablet	Oral use
Malta	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal	25 mg	Tablet	Oral use
Malta	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal	50 mg	Tablet	Oral use

Malta	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal	100 mg	Tablet	Oral use
Malta	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal	2 mg	Dispersible / Chewable Tablet	Oral use
Malta	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal	5 mg	Dispersible / Chewable Tablet	Oral use
Malta	GlaxoSmithKline (Ireland) Ltd Stonemasons Way Rathfarnham Dublin 16 Ireland	Lamictal	25 mg	Dispersible / Chewable Tablet	Oral use
The Netherlands	GlaxoSmithKline BV Huis ter Heideweg 62 3705 LZ Zeist The Netherlands	Lamictal 2 Dispers	2 mg	Dispersible Tablet	Oral use
The Netherlands	GlaxoSmithKline BV Huis ter Heideweg 62 3705 LZ Zeist The Netherlands	Lamictal 5 Dispers	5 mg	Dispersible Tablet	Oral use
The Netherlands	GlaxoSmithKline BV Huis ter Heideweg 62 3705 LZ Zeist The Netherlands	Lamictal 25 Dispers	25 mg	Dispersible Tablet	Oral use

The Netherlands	GlaxoSmithKline BV Huis ter Heideweg 62 3705 LZ Zeist The Netherlands	Lamictal 50 Dispers	50 mg	Dispersible Tablet	Oral use
The Netherlands	GlaxoSmithKline BV Huis ter Heideweg 62 3705 LZ Zeist The Netherlands	Lamictal 100 Dispers	100 mg	Dispersible Tablet	Oral use
The Netherlands	GlaxoSmithKline BV Huis ter Heideweg 62 3705 LZ Zeist The Netherlands	Lamictal 200 Dispers	200 mg	Dispersible Tablet	Oral use
Norway	GlaxoSmithKline AS Forskningsveien 2a Postbox 180 Vinderen N-0319 Oslo Norway	Lamictal	2 mg	Dispersible Tablet	Oral use
Norway	GlaxoSmithKline AS Forskningsveien 2a Postbox 180 Vinderen N-0319 Oslo Norway	Lamictal	5 mg	Dispersible Tablet	Oral use
Norway	GlaxoSmithKline AS Forskningsveien 2a Postbox 180 Vinderen N-0319 Oslo Norway	Lamictal	25 mg	Dispersible Tablet	Oral use
Norway	GlaxoSmithKline AS Forskningsveien 2a Postbox 180 Vinderen N-0319 Oslo Norway	Lamictal	50 mg	Dispersible Tablet	Oral use

Norway	GlaxoSmithKline AS Forskningsveien 2a Postbox 180 Vinderen N-0319 Oslo Norway	Lamictal	100 mg	Dispersible Tablet	Oral use
Norway	GlaxoSmithKline AS Forskningsveien 2a Postbox 180 Vinderen N-0319 Oslo Norway	Lamictal	200 mg	Dispersible Tablet	Oral use
Poland	GlaxoSmithKline Export Ltd 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	Lamitrin	25 mg	Tablet	Oral use
Poland	GlaxoSmithKline Export Ltd 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	Lamitrin	50 mg	Tablet	Oral use
Poland	GlaxoSmithKline Export Ltd 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	Lamitrin	100 mg	Tablet	Oral use
Poland	GlaxoSmithKline Export Ltd 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	Lamitrin S	2 mg	Dispersible Tablet	Oral use

Poland	GlaxoSmithKline Export Ltd 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	Lamitrin S	5 mg	Dispersible Tablet	Oral use
Poland	GlaxoSmithKline Export Ltd 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	Lamitrin S	25 mg	Dispersible Tablet	Oral use
Poland	GlaxoSmithKline Export Ltd 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	Lamitrin S	50 mg	Dispersible Tablet	Oral use
Poland	GlaxoSmithKline Export Ltd 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	Lamitrin S	100 mg	Dispersible Tablet	Oral use
Poland	GlaxoSmithKline Export Ltd 980 Great West Road Brentford Middlesex TW8 9GS United Kingdom	Lamitrin S	200 mg	Dispersible Tablet	Oral use
Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	25 mg	Tablet	Oral use

Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	50 mg	Tablet	Oral use
Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	100 mg	Tablet	Oral use
Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	200 mg	Tablet	Oral use
Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	2 mg	Dispersible Tablet	Oral use

Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	5 mg	Dispersible Tablet	Oral use
Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	25 mg	Dispersible Tablet	Oral use
Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	50 mg	Dispersible Tablet	Oral use
Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	100 mg	Dispersible Tablet	Oral use

Portugal	Laboratórios Wellcome de Portugal Lda. Rua Dr. António Loureiro Borges 3 Arquiparque - Miraflores 1495 - 131 Algés Portugal	Lamictal	200 mg	Dispersible Tablet	Oral use
Romania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 25 mg	25 mg	Tablet	Oral use
Romania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 50 mg	50 mg	Tablet	Oral use
Romania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 100 mg	100 mg	Tablet	Oral use

Romania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 2 mg	2 mg	Dispersible/Chewable Tablet	Oral use
Romania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 5 mg	5 mg	Dispersible/Chewable Tablet	Oral use
Romania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 25 mg	25 mg	Dispersible/Chewable Tablet	Oral use
Romania	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom	Lamictal 100 mg	100 mg	Dispersible/Chewable Tablet	Oral use
Slovakia	GlaxoSmithKline Slovakia s.r.o. Galvaniho 7/A 82104 Bratislava Slovakia	Lamictal 25 mg	25 mg	Tablet	Oral use

Slovakia	GlaxoSmithKline Slovakia s.r.o. Galvaniho 7/A 82104 Bratislava Slovakia	Lamictal 50 mg	50 mg	Tablet	Oral use
Slovakia	GlaxoSmithKline Slovakia s.r.o. Galvaniho 7/A 82104 Bratislava Slovakia	Lamictal 100 mg	100 mg	Tablet	Oral use
Slovakia	GlaxoSmithKline Slovakia s.r.o. Galvaniho 7/A 82104 Bratislava Slovakia	Lamictal 2 mg	2 mg	Dispersible Tablet	Oral use
Slovakia	GlaxoSmithKline Slovakia s.r.o. Galvaniho 7/A 82104 Bratislava Slovakia	Lamictal 5 mg	5 mg	Dispersible Tablet	Oral use
Slovakia	GlaxoSmithKline Slovakia s.r.o. Galvaniho 7/A 82104 Bratislava Slovakia	Lamictal 25 mg	25 mg	Dispersible Tablet	Oral use
Slovakia	GlaxoSmithKline Slovakia s.r.o. Galvaniho 7/A 82104 Bratislava Slovakia	Lamictal 100 mg	100 mg	Dispersible Tablet	Oral use
Slovenia	GSK d.o.o. Ljubljana Knezov stradon 90 1000 Ljubljana Slovenia	Lamictal 25 mg tablete	25 mg	Tablet	Oral use
Slovenia	GSK d.o.o. Ljubljana Knezov stradon 90 1000 Ljubljana Slovenia	Lamictal 50 mg tablete	50 mg	Tablet	Oral use

Slovenia	GSK d.o.o. Ljubljana Knezov stradon 90 1000 Ljubljana Slovenia	Lamictal 100 mg tablete	100 mg	Tablet	Oral use
Slovenia	GSK d.o.o. Ljubljana Knezov stradon 90 1000 Ljubljana Slovenia	Lamictal 200 mg tablete	200 mg	Tablet	Oral use
Slovenia	GSK d.o.o. Ljubljana Knezov stradon 90 1000 Ljubljana Slovenia	Lamictal 5 mg disperzibilne/žvečljive tablete	5 mg	Dispersible/Chewable Tablet	Oral use
Slovenia	GSK d.o.o. Ljubljana Knezov stradon 90 1000 Ljubljana Slovenia	Lamictal 25 mg disperzibilne/žvečljive tablete	25 mg	Dispersible/Chewable Tablet	Oral use
Slovenia	GSK d.o.o. Ljubljana Knezov stradon 90 1000 Ljubljana Slovenia	Lamictal 50 mg disperzibilne/žvečljive tablete	50 mg	Dispersible/Chewable Tablet	Oral use
Slovenia	GSK d.o.o. Ljubljana Knezov stradon 90 1000 Ljubljana Slovenia	Lamictal 100 mg disperzibilne/žvečljive tablete	100 mg	Dispersible/Chewable Tablet	Oral use
Slovenia	GSK d.o.o. Ljubljana Knezov stradon 90 1000 Ljubljana Slovenia	Lamictal 200 mg disperzibilne/žvečljive tablete	200 mg	Dispersible/Chewable Tablet	Oral use
Spain	GlaxoSmithKline S.A Severo Ochoa 2 28760 Tres Cantos Madrid Spain	Lamictal	50 mg	Tablet	Oral use

Spain	GlaxoSmithKline S.A Severo Ochoa 2 28760 Tres Cantos Madrid Spain	Lamictal	100 mg	Tablet	Oral use
Spain	GlaxoSmithKline S.A Severo Ochoa 2 28760 Tres Cantos Madrid Spain	Lamictal	200 mg	Tablet	Oral use
Spain	GlaxoSmithKline S.A Severo Ochoa 2 28760 Tres Cantos Madrid Spain	Lamictal	2 mg	Dispersible Tablet	Oral use
Spain	GlaxoSmithKline S.A Severo Ochoa 2 28760 Tres Cantos Madrid Spain	Lamictal	5 mg	Dispersible Tablet	Oral use
Spain	GlaxoSmithKline S.A Severo Ochoa 2 28760 Tres Cantos Madrid Spain	Lamictal	25 mg	Dispersible Tablet	Oral use
Spain	GlaxoSmithKline S.A Severo Ochoa 2 28760 Tres Cantos Madrid Spain	Lamictal	50 mg	Dispersible Tablet	Oral use
Spain	GlaxoSmithKline S.A Severo Ochoa 2 28760 Tres Cantos Madrid Spain	Lamictal	100 mg	Dispersible Tablet	Oral use
Spain	GlaxoSmithKline S.A Severo Ochoa 2 28760 Tres Cantos Madrid Spain	Lamictal	200 mg	Dispersible Tablet	Oral use

Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	25 mg	Tablet	Oral use
Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	50 mg	Tablet	Oral use
Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	100 mg	Tablet	Oral use
Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	200 mg	Tablet	Oral use
Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	2 mg	Soluble Tablet	Oral use
Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	5 mg	Soluble Tablet	Oral use

Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	25 mg	Soluble Tablet	Oral use
Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	50 mg	Soluble Tablet	Oral use
Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	100 mg	Soluble Tablet	Oral use
Sweden	GlaxoSmithKline AB Box 516 169 29 Solna Sweden	Lamictal	200 mg	Soluble Tablet	Oral use
United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	25 mg	Tablet	Oral use

United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	50 mg	Tablet	Oral use
United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	100 mg	Tablet	Oral use

United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	200 mg	Tablet	Oral use
United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	2 mg	Dispersible Tablet	Oral use

United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	5 mg	Dispersible Tablet	Oral use
United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	25 mg	Dispersible Tablet	Oral use

United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	50 mg	Dispersible Tablet	Oral use
United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	100 mg	Dispersible Tablet	Oral use

United Kingdom	The Wellcome Foundation Limited Glaxo Wellcome House Berkeley Avenue Greenford, Middlesex UB6 0NN United Kingdom *Trading as* *GlaxoSmithKline UK* *Stockley Park West* *Uxbridge* *Middlesex UB11 1BT* *United Kingdom*	Lamictal	200 mg	Dispersible Tablet	Oral use

ANNEX II

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARIES OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS

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

Lamotrigine (the active substance of Lamictal) is a well-known anti-epileptic agent approved for the treatment of epileptic seizures in most EU-member states on a National basis. It is indicated as monotherapy as well as adjuvant therapy in partial seizures with or without secondary generalisation, primary generalised seizures and some specific seizure types. In addition Lamictal has been approved for use in bipolar patients in several EU member states except in the UK, Netherlands, France and Cyprus.

Apart from the indication in bipolar disorder the SPC of Lamictal in the different EU members show a large overlap. Nevertheless differences exist with respect to the precise wording of the epilepsy indication, restriction of age-categories, seizure types, dose recommendations and interactions.

Hence an article 30 procedure (Directive 2001/83/EC) for harmonisation of the SPC of lamotrigine across Europe has been initiated by the Marketing Authorisation Holder. This referral is undertaken following concerns related to divergent decisions on approval of the bipolar indication for lamotrigine across EU Member States.

The main areas of disharmony of the existing Summary of Product Characteristics concerned the Therapeutic Indications.
In addition, the assessment of quality issues has led to the harmonisation of the pharmaceutical forms (tablet and dispersible/chewable tablet) across the EU.

Therapeutic Indications (SPC section 4.1)

Epilepsy

"Adults and children above 12 years
{Tradename} is indicated for use as adjunctive or monotherapy in the treatment of epilepsy, for partial seizures and generalised seizures, including tonic-clonic seizures and the seizures associated with Lennox-Gastaut Syndrome".
The age range will be modified to reflect the ages for which supporting data are available, adults and patients aged 13 years and older (adolescents). Monotherapy in Lennox-Gastaut Syndrome is rarely achievable, as usually more than one medicinal product is needed to control the symptoms. The indication will specify that the target population is "Adults and adolescents aged 13 years and above".

"Children 2 to 12 years
{Tradename} is indicated as adjunctive therapy in the treatment of epilepsy, for partial seizures and generalised seizures including tonic-clonic seizures and the seizures associated with Lennox-Gastaut Syndrome".
The age range will be modified considering that patients aged 12 years fall within the definition of adolescents. Efficacy as monotherapy treatment of typical absence seizures was demonstrated.
The indication will specify that the target population is "Children and adolescents aged 2 to 12 years".

"After epileptic control has been achieved during adjunctive therapy, concomitant antiepileptic drugs (AEDs) may be withdrawn and patients continued on {Tradename} monotherapy".
The CHMP concluded that conversion to monotherapy is not an indication but information on correct use of the product. This text should be therefore moved to section 4.2, Posology and method of administration.

Bipolar disorder

"Adults 18 years and above
{Tradename} is indicated for the prevention of mood episodes in patients with bipolar disorder, predominantly by preventing depressive episodes".
The CHMP was of the opinion that lamotrigine is effective in preventing one aspect of mood episodes in Bipolar disorder, depressive episodes, while prevention of manic or hypomanic episodes has not been proven. It should be also underlined that lamotrigine is not indicated for acute treatment. The target population will be Bipolar I patients, as these patients were included in the clinical studies.

- Quality aspects

The drug substance and the drug product have been appropriately described and generally satisfactory documentation has been provided. The excipients used in the formulations of the drug product and manufacturing processes are standard for the proposed pharmaceutical forms. The results indicate that the drug substance and drug product can be reproducibly manufactured.

- Clinical aspects

Epilepsy

The use of lamotrigine in the proposed harmonised indications has been generally well substantiated according to the available clinical data submitted by the Marketing Authorisation Holder.

The benefit/risk ratio of adjunctive treatment of partial and generalised seizures in adults and adolescents aged 13 years and above, was confirmed to be positive.

Although the Marketing Authorisation Holder has not conducted specific studies with lamotrigine monotherapy solely in patients with primary generalised tonic clonic seizures, data from controlled initial monotherapy studies (studies UK49/89, UK74) reassure on the efficacy of lamotrigine on this seizure types.
The benefit/risk of lamotrigine as add-on treatment in primary generalised tonic clonic seizures in children is also considered favourable.

Lennox-Gastaut Syndrome is a difficult to treat condition and monotherapy is rarely achieved. Treatment is initiated as monotherapy, but almost inevitably soon other antiepileptics will be added to control the symptoms. There is no consensus on which drug should be used as initial treatment; however, the data analysed do not exclude that lamotrigine could be the initial agent.

The maintenance effect on typical absence seizures remains unclear, thus a warning will be included in the SPC stating that "*In children taking lamotrigine for the treament of typical absence seizures, efficacy may not be maintained in all patients".*

Bipolar Disorder

The CHMP was concerned about the suitability of lamotrigine used as mood stabiliser. In fact, according to available data the mood stabilising property of lamotrigine appears to be due to the prevention of depressive episodes and not to the prevention of manic episodes. A mood stabilising claim implies the protection from both manic and depressive episodes. The prevention of recurrence of both type of episodes has not been shown for lamotrigine. In addition, the patients studied were diagnosed with Bipolar I disorder; therefore the results of these studies may not be extrapolated to Bipolar II disorder.

A CNS Scientific Advisory Group (SAG) was also consulted to advise the CHMP on Bipolar disorder and its treatment. Specifically, the SAG was asked to clarify the definition of a mood stabiliser and the need for a medicinal product to act on both poles of the disorders. Also, the current standard treatments for Bipolar disorder and the feasibility of monotherapy were discussed.
The group concurred that theoretically a mood stabiliser should be able to prevent both manic and depressive recurrences, the characteristic features of Bipolar Disorder, but as of now we do not possess such an ideal mood stabiliser. Although the disorder is a heterogeneous disease with contrasting therapeutic needs, it was recognised that depressive aspect is the most worrying and a drug able to prevent depressive episodes is therefore of value.
In the clinical practice, the approved drugs for Bipolar disorder generally need to be combined to achieve an acceptable control of the symptoms. Monotherapy should be the most desirable achievement, as the safety concerns tend to be reduced when only one drug is used, but at the present it is rarely obtained. Usually treatment is started as monotherapy; then if the control of the symptoms is not reached, other medicines are added based on the experience of the physician.

The CHMP, taking into consideration the assessment of the studies and the recommendation of the SAG concluded that lamotrigine should be used for the prevention of depressive episode in patients with Bipolar I disorder who experience predominantly depressive episodes. As the efficacy has been demonstrated for prevention of recurrence only, lamotrigine is not indicated for the acute treatment of manic or depressive episodes.

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

Whereas

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

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

- The CHMP concluded that the data are supportive of the following indications:

"Epilepsy

Adults and adolescents aged 13 years and above
- Adjunctive or monotherapy treatment of partial seizures and generalised seizures, including tonic-clonic seizures.
- Seizures associated with Lennox-Gastaut syndrome. Lamictal is given as adjunctive therapy but may be the initial antiepileptic drug (AED) to start with in Lennox-Gastaut syndrome.

Children and adolescents aged 2 to 12 years
- Adjunctive treatment of partial seizures and generalised seizures, including tonic-clonic seizures and the seizures associated with Lennox-Gastaut syndrome.
- Monotherapy of typical absence seizures.

Bipolar disorder

Adults aged 18 years and above
- Prevention of depressive episodes in patients with bipolar I disorder who experience predominantly depressive episodes (see section 5.1).

Lamictal is not indicated for the acute treatment of manic or depressive episodes".

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

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 25 mg tablets.
Lamictal and associated names (see Annex I) 50 mg tablets.
Lamictal and associated names (see Annex I) 100 mg tablets.
Lamictal and associated names (see Annex I) 200 mg tablets.

Lamictal and associated names (see Annex I) 2 mg dispersible/chewable tablets.
Lamictal and associated names (see Annex I) 5 mg dispersible/chewable tablets.
Lamictal and associated names (see Annex I) 25 mg dispersible/chewable tablets.
Lamictal and associated names (see Annex I) 50 mg dispersible/chewable tablets.
Lamictal and associated names (see Annex I) 100 mg dispersible/chewable tablets.
Lamictal and associated names (see Annex I) 200 mg dispersible/chewable tablets.

[See Annex I - To be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each Lamictal 25 mg tablet contains 25 mg lamotrigine.
Excipient: Each tablet contains 23.5 mg lactose.
Each Lamictal 50 mg tablet contains 50 mg lamotrigine.
Excipient: Each tablet contains 46.9 mg lactose.
Each Lamictal 100 mg tablet contains 100 mg lamotrigine.
Excipient: Each tablet contains 93.9 mg lactose.
Each Lamictal 200 mg tablet contains 200 mg lamotrigine.
Excipient: Each tablet contains 109.0 mg lactose.

Each Lamictal 2 mg dispersible/chewable tablet contains 2 mg lamotrigine.
Each Lamictal 5 mg dispersible/chewable tablet contains 5 mg lamotrigine.
Each Lamictal 25 mg dispersible/chewable tablet contains 25 mg lamotrigine.
Each Lamictal 50 mg dispersible/chewable tablet contains 50 mg lamotrigine.
Each Lamictal 100 mg dispersible/chewable tablet contains 100 mg lamotrigine.
Each Lamictal 200 mg dispersible/chewable tablet contains 200 mg lamotrigine.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet.
Dispersible/chewable tablet.

25 mg tablets:
Pale, yellowish-brown, multifaceted, super-elliptical tablet, marked “GSEC7” on one side and “25” on the other.

50 mg tablets:
Pale, yellowish-brown, multifaceted, super-elliptical tablet, marked “GSEE1” on one side and “50” on the other.

100 mg tablets:
Pale, yellowish-brown, multifaceted, super-elliptical tablet, marked “GSEE5” on one side and “100” on the other.

200 mg tablets:
Pale, yellowish-brown, multifaceted, super-elliptical tablet, marked “GSEE7” on one side and “200” on the other.

2 mg dispersible/chewable tablets:
White to off-white round tablet with a blackcurrant odour. One side has a bevelled edge and is marked “LTG” above the number 2. The other side is marked with two overlapping super-ellipses at right angles. The tablets may be slightly mottled.

5 mg dispersible/chewable tablets:
White to off-white, elongated, biconvex tablet with a blackcurrant odour, marked “GS CL2” on one side and “5” on the other. The tablets may be slightly mottled.

25 mg dispersible/chewable tablets:
White to off-white multi-faceted, super-elliptical, tablet with a blackcurrant odour, marked “GSCL5” on one side “25” on the other. The tablets may be slightly mottled.

50 mg dispersible/chewable tablets:
White to off-white multi-faceted, super-elliptical, tablet with a blackcurrant odour, marked “GSCX7” on one side and “50” on the other. The tablets may be slightly mottled.

100 mg dispersible/chewable tablets:
White to off-white multi-faceted, super-elliptical, tablet with a blackcurrant odour, marked “GSCL7” on one side and “100” on the other. The tablets may be slightly mottled.

200 mg dispersible/chewable tablets:
White to off-white multi-faceted, super-elliptical, tablet with a blackcurrant odour, marked “GSEC5” on one side and “200” on the other. The tablets may be slightly mottled.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Epilepsy

Adults and adolescents aged 13 years and above

- Adjunctive or monotherapy treatment of partial seizures and generalised seizures, including tonic-clonic seizures.
- Seizures associated with Lennox-Gastaut syndrome. Lamictal is given as adjunctive therapy but may be the initial antiepileptic drug (AED) to start with in Lennox-Gastaut syndrome.

Children and adolescents aged 2 to 12 years

- Adjunctive treatment of partial seizures and generalised seizures, including tonic-clonic seizures and the seizures associated with Lennox-Gastaut syndrome.
- Monotherapy of typical absence seizures.

Bipolar disorder

Adults aged 18 years and above

- Prevention of depressive episodes in patients with bipolar I disorder who experience predominantly depressive episodes (see section 5.1).

Lamictal is not indicated for the acute treatment of manic or depressive episodes.

4.2 Posology and method of administration

Lamictal tablets should be swallowed whole, and should not be chewed or crushed.

Lamictal dispersible/chewable tablets may be chewed, dispersed in a small volume of water (at least enough to cover the whole tablet) or swallowed whole with a little water.

If the calculated dose of lamotrigine (for example for treatment of children with epilepsy or patients with hepatic impairment) does not equate to whole tablets, the dose to be administered is that equal to the lower number of whole tablets.

Restarting therapy

Prescribers should assess the need for escalation to maintenance dose when restarting Lamictal in patients who have discontinued Lamictal for any reason, since the risk of serious rash is associated with high initial doses and exceeding the recommended dose escalation for lamotrigine (see section 4.4). The greater the interval of time since the previous dose, the more consideration should be given to escalation to the maintenance dose. When the interval since discontinuing lamotrigine exceeds five half-lives (see section 5.2), Lamictal should generally be escalated to the maintenance dose according to the appropriate schedule.

It is recommended that Lamictal not be restarted in patients who have discontinued due to rash associated with prior treatment with lamotrigine unless the potential benefit clearly outweighs the risk.

Epilepsy

The recommended dose escalation and maintenance doses for adults and adolescents aged 13 years and above (Table 1) and for children and adolescents aged 2 to 12 years (Table 2) are given below. Because of a risk of rash the initial dose and subsequent dose escalation should not be exceeded (see section 4.4).

When concomitant AEDs are withdrawn or other AEDs/medicinal products are added on to treatment regimes containing lamotrigine, consideration should be given to the effect this may have on lamotrigine pharmacokinetics (see section 4.5).

Table 1: Adults and adolescents aged 13 years and above – recommended treatment regimen in epilepsy

Treatment regimen	Weeks 1 + 2	Weeks 3 + 4	Usual maintenance dose
Monotherapy:	25 mg/day (once a day)	50 mg/day (once a day)	100 − 200 mg/day (once a day or two divided doses) To achieve maintenance, doses may be increased by maximum of 50 - 100 mg every one to two weeks until optimal response is achieved 500 mg/day has been required by some patients to achieve desired response
Adjunctive therapy WITH valproate (inhibitor of lamotrigine glucuronidation – see section 4.5)**:**			
This dosage regimen should be used with valproate regardless of any concomitant medicinal products	12.5 mg/day (given as 25 mg on alternate days)	25 mg/day (once a day)	100 − 200 mg/day (once a day or two divided doses) To achieve maintenance, doses may be increased by maximum of 25 - 50 mg every one to two weeks until optimal response is achieved
Adjunctive therapy WITHOUT valproate and WITH inducers of lamotrigine glucuronidation (see section 4.5)**:**			
This dosage regimen should be used without valproate but with: phenytoin carbamazepine phenobarbitone primidone rifampicin lopinavir/ritonavir	50 mg/day (once a day)	100 mg/day (two divided doses)	200 − 400 mg/day (two divided doses) To achieve maintenance, doses may be increased by maximum of 100 mg every one to two weeks until optimal response is achieved 700 mg/day has been required by some patients to achieve desired response
Adjunctive therapy WITHOUT valproate and WITHOUT inducers of lamotrigine glucuronidation (see section 4.5)**:**			
This dosage regimen should be used with other medicinal products that do not significantly inhibit or induce lamotrigine glucuronidation	25 mg/day (once a day)	50 mg/day (once a day)	100 − 200 mg/day (once a day or two divided doses) To achieve maintenance, doses may be increased by maximum of 50 - 100 mg every one to two weeks until optimal response is achieved
In patients taking medicinal products where the pharmacokinetic interaction with lamotrigine is currently not known (see section 4.5), the treatment regimen as recommended for lamotrigine with concurrent valproate should be used.			

Table 2: Children and adolescents aged 2 to 12 years - recommended treatment regimen in epilepsy (total daily dose in mg/kg body weight/day)

Treatment regimen	Weeks 1 + 2	Weeks 3 + 4	Usual maintenance dose
Monotherapy of typical absence seizures:	0.3 mg/kg/day (once a day or two divided doses)	0.6 mg/kg/day (once a day or two divided doses)	1 – 10 mg/kg/day, although some patients have required higher doses (up to 15 mg/kg/day) to achieve desired response (once a day or two divided doses) To achieve maintenance, doses may be increased by maximum of 0.6 mg/kg/day every one to two weeks until optimal response is achieved
Adjunctive therapy WITH valproate (inhibitor of lamotrigine glucuronidation – see section 4.5)**:**			
This dosage regimen should be used with valproate regardless of any other concomitant medicinal products	0.15 mg/kg/day* (once a day)	0.3 mg/kg/day (once a day)	1 − 5 mg/kg/day (once a day or two divided doses) To achieve maintenance, doses may be increased by maximum of 0.3 mg/kg every one to two weeks until optimal response is achieved, with a maximum maintenance dose of 200 mg/day
Adjunctive therapy WITHOUT valproate and WITH inducers of lamotrigine glucuronidation (see section 4.5)**:**			
This dosage regimen should be used without valproate but with: phenytoin carbamazepine phenobarbitone primidone rifampicin lopinavir/ritonavir	0.6 mg/kg/day (two divided doses)	1.2 mg/kg/day (two divided doses)	5 − 15 mg/kg/day (once a day or two divided doses) To achieve maintenance, doses may be increased by maximum of 1.2 mg/kg every one to two weeks until optimal response is achieved, with a maximum maintenance dose of 400 mg/day
Adjunctive therapy WITHOUT valproate and WITHOUT inducers of lamotrigine glucuronidation (see section 4.5)**:**			
This dosage regimen should be used with other medicinal products that do not significantly inhibit or induce lamotrigine glucuronidation	0.3 mg/kg/day (once a day or two divided doses)	0.6 mg/kg/day (once a day or two divided doses)	1 − 10 mg/kg/day (once a day or two divided doses) To achieve maintenance, doses may be increased by maximum of 0.6 mg/kg every one to two weeks until optimal response is achieved, with a maximum of maintenance dose of 200 mg/day
In patients taking medicinal products where the pharmacokinetic interaction with lamotrigine is currently not known (see section 4.5), the treatment regimen as recommended for lamotrigine with concurrent valproate should be used.			
2 mg dispersible/chewable tablets - where this is the lowest marketed strength: <* If the calculated daily dose in patients taking valproate is 1 mg or more but less than 2 mg, then Lamictal 2 mg dispersible/chewable tablets may be taken on alternate days for the first two weeks. If the calculated daily dose in patients taking valproate is less than 1 mg, then Lamictal should not be administered.>			

5 mg dispersible/chewable tablets - where 2 mg dispersible/chewable tablets are not marketed and Lamictal 5 mg dispersible/chewable tablets are the lowest marketed strength:
<* If the calculated daily dose in patients taking valproate is 2.5 mg or more but less than 5 mg, then Lamictal 5 mg dispersible/chewable tablets may be taken on alternate days for the first two weeks. If the calculated daily dose in patients taking valproate is less than 2.5 mg, then Lamictal should not be administered.>

To ensure a therapeutic dose is maintained the weight of a child must be monitored and the dose reviewed as weight changes occur. It is likely that patients aged two to six years will require a maintenance dose at the higher end of the recommended range.

If epileptic control is achieved with adjunctive treatment, concomitant AEDs may be withdrawn and patients continued on Lamictal monotherapy.

5 mg dispersible/chewable tablets – where 2 mg dispersible/chewable tablets are not marketed and 5 mg dispersible/chewable tablets are the lowest marketed strength:
<It should be noted that with the currently available Lamictal 5 mg dispersible/chewable tablet strength, it is not possible to accurately initiate lamotrigine therapy using the recommended dosing guidelines in paediatric patients weighing less than 17 kg.>

Children below 2 years
There are limited data on the efficacy and safety of lamotrigine for adjunctive therapy of partial seizures in children aged 1 month to 2 years (see section 4.4). There are no data in children below 1 month of age. Thus Lamictal is not recommended for use in children below 2 years of age. If, based on clinical need, a decision to treat is nevertheless taken, see sections 4.4, 5.1 and 5.2.

Bipolar disorder

The recommended dose escalation and maintenance doses for adults of 18 years of age and above are given in the tables below. The transition regimen involves escalating the dose of lamotrigine to a maintenance stabilisation dose over six weeks (Table 3) after which other psychotropic medicinal products and/or AEDs can be withdrawn, if clinically indicated (Table 4). The dose adjustments following addition of other psychotropic medicinal products and/or AEDs are also provided below (Table 5). Because of the risk of rash the initial dose and subsequent dose escalation should not be exceeded (see section 4.4).

Table 3: Adults aged 18 years and above - recommended dose escalation to the maintenance total daily stabilisation dose in treatment of bipolar disorder

Treatment Regimen	Weeks 1 + 2	Weeks 3 + 4	Week 5	Target Stabilisation Dose (Week 6)*
Monotherapy with lamotrigine OR adjunctive therapy WITHOUT valproate and WITHOUT inducers of lamotrigine glucuronidation (see section 4.5)**:**				
This dosage regimen should be used with other medicinal products that do not significantly inhibit or induce lamotrigine glucuronidation	25 mg/day (once a day)	50 mg/day (once a day or two divided doses)	100 mg/day (once a day or two divided doses)	200 mg/day - usual target dose for optimal response (once a day or two divided doses) Doses in the range 100 - 400 mg/day used in clinical trials
Adjunctive therapy WITH valproate (inhibitor of lamotrigine glucuronidation – see section 4.5)**:**				
This dosage regimen should be used with valproate regardless of any concomitant medicinal products	12.5 mg/day (given as 25 mg on alternate days)	25 mg/day (once a day)	50 mg/day (once a day or two divided doses)	100 mg/day - usual target dose for optimal response (once a day or two divided doses) Maximum dose of 200 mg/day can be used depending on clinical response
Adjunctive therapy WITHOUT valproate and WITH inducers of lamotrigine glucuronidation (see section 4.5)**:**				
This dosage regimen should be used without valproate but with: phenytoin carbamazepine phenobarbitone primidone rifampicin lopinavir/ritonavir	50 mg/day (once a day)	100 mg/day (two divided doses)	200 mg/day (two divided doses)	300 mg/day in week 6, if necessary increasing to usual target dose of 400 mg/day in week 7, to achieve optimal response (two divided doses)
In patients taking medicinal products where the pharmacokinetic interaction with lamotrigine is currently not known (see section 4.5), the dose escalation as recommended for lamotrigine with concurrent valproate, should be used.				

* The Target stabilisation dose will alter depending on clinical response

Table 4: Adults aged 18 years and above - maintenance stabilisation total daily dose following withdrawal of concomitant medicinal products in treatment of bipolar disorder

Once the target daily maintenance stabilisation dose has been achieved, other medicinal products may be withdrawn as shown below.

Treatment Regimen	Current lamotrigine stabilisation dose (prior to withdrawal)	Week 1 (beginning with withdrawal)	Week 2	Week 3 onwards *
Withdrawal of valproate (inhibitor of lamotrigine glucuronidation – see section 4.5), depending on original dose of lamotrigine**:**				
When valproate is withdrawn, double the stabilisation dose, not exceeding an increase of more than 100 mg/week	100 mg/day	200 mg/day	Maintain this dose (200 mg/day) (two divided doses)	
	200 mg/day	300 mg/day	400 mg/day	Maintain this dose (400 mg/day)
Withdrawal of inducers of lamotrigine glucuronidation (see section 4.5), depending on original dose of lamotrigine**:**				
This dosage regimen should be used when the following are withdrawn: phenytoin carbamazepine phenobarbitone primidone rifampicin lopinavir/ritonavir	400 mg/day	400 mg/day	300 mg/day	200 mg/day
	300 mg/day	300 mg/day	225 mg/day	150 mg/day
	200 mg/day	200 mg/day	150 mg/day	100 mg/day
Withdrawal of medicinal products that do NOT significantly inhibit or induce lamotrigine glucuronidation (see section 4.5)**:**				
This dosage regimen should be used when other medicinal products that do not significantly inhibit or induce lamotrigine glucuronidation are withdrawn	Maintain target dose achieved in dose escalation (200 mg/day; two divided doses) (dose range 100 - 400 mg/day)			
In patients taking medicinal products where the pharmacokinetic interaction with lamotrigine is currently not known (see section 4.5), the treatment regimen as recommended for lamotrigine with concurrent valproate, should be used.				

* Dose may be increased to 400 mg/day as needed

Table 5: Adults aged 18 years and above - adjustment of lamotrigine daily dosing following the addition of other medicinal products in treatment of bipolar disorder

There is no clinical experience in adjusting the lamotrigine daily dose following the addition of other medicinal products. However, based on interaction studies with other medicinal products, the following recommendations can be made:

Treatment Regimen	Current lamotrigine stabilisation dose (prior to addition)	Week 1 (beginning with addition)	Week 2	Week 3 onwards
Addition of valproate (inhibitor of lamotrigine glucuronidation – see section 4.5), depending on original dose of lamotrigine**:**				
This dosage regimen should be used when valproate is added regardless of any concomitant medicinal products	200 mg/day	100 mg/day	Maintain this dose (100 mg/day)	
	300 mg/day	150 mg/day	Maintain this dose (150 mg/day)	
	400 mg/day	200 mg/day	Maintain this dose (200 mg/day)	
Addition of inducers of lamotrigine glucuronidation in patients NOT taking valproate (see section 4.5), depending on original dose of lamotrigine**:**				
This dosage regimen should be used when the following are added without valproate: phenytoin carbamazepine phenobarbitone primidone rifampicin lopinavir/ritonavir	200 mg/day	200 mg/day	300 mg/day	400 mg/day
	150 mg/day	150 mg/day	225 mg/day	300 mg/day
	100 mg/day	100 mg/day	150 mg/day	200 mg/day
Addition of medicinal products that do NOT significantly inhibit or induce lamotrigine glucuronidation (see section 4.5)**:**				
This dosage regimen should be used when other medicinal products that do not significantly inhibit or induce lamotrigine glucuronidation are added	Maintain target dose achieved in dose escalation (200 mg/day; dose range 100-400 mg/day)			
In patients taking medicinal products where the pharmacokinetic interaction with lamotrigine is currently not known (see section 4.5), the treatment regimen as recommended for lamotrigine with concurrent valproate, should be used.				

Discontinuation of Lamictal in patients with bipolar disorder

In clinical trials, there was no increase in the incidence, severity or type of adverse reactions following abrupt termination of lamotrigine versus placebo. Therefore, patients may terminate Lamictal without a step-wise reduction of dose.

Children and adolescents below 18 years

Lamictal is not recommended for use in children below 18 years of age due to a lack of data on safety and efficacy (see section 4.4).

General dosing recommendations for Lamictal in special patient populations

Women taking hormonal contraceptives
The use of an ethinyloestradiol/levonorgestrel (30 μg/150 μg) combination increases the clearance of lamotrigine by approximately two-fold, resulting in decreased lamotrigine levels. Following titration, higher maintenance doses of lamotrigine (by as much as two-fold) may be needed to attain a maximal therapeutic response. During the pill-free week, a two-fold increase in lamotrigine levels has been observed. Dose-related adverse events cannot be excluded. Therefore, consideration should be given to using contraception without a pill-free week, as first-line therapy (for example, continuous hormonal contraceptives or non-hormonal methods; see sections 4.4 and 4.5).

Starting hormonal contraceptives in patients already taking maintenance doses of lamotrigine and NOT taking inducers of lamotrigine glucuronidation
The maintenance dose of lamotrigine will in most cases need to be increased by as much as two-fold (see sections 4.4 and 4.5). It is recommended that from the time that the hormonal contraceptive is started, the lamotrigine dose is increased by 50 to 100 mg/day every week, according to the individual clinical response. Dose increases should not exceed this rate, unless the clinical response supports larger increases. Measurement of serum lamotrigine concentrations before and after starting hormonal contraceptives may be considered, as confirmation that the baseline concentration of lamotrigine is being maintained. If necessary, the dose should be adapted. In women taking a hormonal contraceptive that includes one week of inactive treatment ("pill-free week"), serum lamotrigine level monitoring should be conducted during week 3 of active treatment, i.e. on days 15 to 21 of the pill cycle. Therefore, consideration should be given to using contraception without a pill-free week, as first-line therapy (for example, continuous hormonal contraceptives or non-hormonal methods; see sections 4.4 and 4.5).

Stopping hormonal contraceptives in patients already taking maintenance doses of lamotrigine and NOT taking inducers of lamotrigine glucuronidation
The maintenance dose of lamotrigine will in most cases need to be decreased by as much as 50% (see sections 4.4 and 4.5). It is recommended to gradually decrease the daily dose of lamotrigine by 50-100 mg each week (at a rate not exceeding 25% of the total daily dose per week) over a period of 3 weeks, unless the clinical response indicates otherwise. Measurement of serum lamotrigine concentrations before and after stopping hormonal contraceptives may be considered, as confirmation that the baseline concentration of lamotrigine is being maintained. In women who wish to stop taking a hormonal contraceptive that includes one week of inactive treatment ("pill-free week"), serum lamotrigine level monitoring should be conducted during week 3 of active treatment, i.e. on days 15 to 21 of the pill cycle. Samples for assessment of lamotrigine levels after permanently stopping the contraceptive pill should not be collected during the first week after stopping the pill.

Starting lamotrigine in patients already taking hormonal contraceptives
Dose escalation should follow the normal dose recommendation described in the tables.

Starting and stopping hormonal contraceptives in patients already taking maintenance doses of lamotrigine and TAKING inducers of lamotrigine glucuronidation
Adjustment to the recommended maintenance dose of lamotrigine may not be required.

Elderly (above 65 years)
No dosage adjustment from the recommended schedule is required. The pharmacokinetics of lamotrigine in this age group do not differ significantly from a non-elderly adult population (see section 5.2).

Renal impairment
Caution should be exercised when administering Lamictal to patients with renal failure. For patients with end-stage renal failure, initial doses of lamotrigine should be based on patients' concomitant medicinal products; reduced maintenance doses may be effective for patients with significant renal functional impairment (see sections 4.4 and 5.2).

Hepatic impairment
Initial, escalation and maintenance doses should generally be reduced by approximately 50% in patients with moderate (Child-Pugh grade B) and 75% in severe (Child-Pugh grade C) hepatic impairment. Escalation and maintenance doses should be adjusted according to clinical response (see section 5.2).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

Skin rash

There have been reports of adverse skin reactions, which have generally occurred within the first eight weeks after initiation of lamotrigine treatment. The majority of rashes are mild and self-limiting, however serious rashes requiring hospitalisation and discontinuation of lamotrigine have also been reported. These have included potentially life-threatening rashes such as Stevens–Johnson syndrome and toxic epidermal necrolysis (see section 4.8).

In adults enrolled in studies utilizing the current lamotrigine dosing recommendations the incidence of serious skin rashes is approximately 1 in 500 in epilepsy patients. Approximately half of these cases have been reported as Stevens–Johnson syndrome (1 in 1000). In clinical trials in patients with bipolar disorder, the incidence of serious rash is approximately 1 in 1000.

The risk of serious skin rashes in children is higher than in adults. Available data from a number of studies suggest the incidence of rashes associated with hospitalisation in epileptic children is from 1 in 300 to 1 in 100.

In children, the initial presentation of a rash can be mistaken for an infection, physicians should consider the possibility of a reaction to lamotrigine treatment in children that develop symptoms of rash and fever during the first eight weeks of therapy.

Additionally the overall risk of rash appears to be strongly associated with:

- high initial doses of lamotrigine and exceeding the recommended dose escalation of lamotrigine therapy (see section 4.2)
- concomitant use of valproate (see section 4.2).

Caution is also required when treating patients with a history of allergy or rash to other AEDs as the frequency of non-serious rash after treatment with lamotrigine was approximately three times higher in these patients than in those without such history.

All patients (adults and children) who develop a rash should be promptly evaluated and Lamictal withdrawn immediately unless the rash is clearly not related to lamotrigine treatment. It is recommended that Lamictal not be restarted in patients who have discontinued due to rash associated with prior treatment with lamotrigine unless the potential benefit clearly outweighs the risk.

Rash has also been reported as part of a hypersensitivity syndrome associated with a variable pattern of systemic symptoms including fever, lymphadenopathy, facial oedema and abnormalities of the blood and liver (see section 4.8). The syndrome shows a wide spectrum of clinical severity and may, rarely, lead to disseminated intravascular coagulation and multiorgan failure. It is important to note that early manifestations of hypersensitivity (for example fever, lymphadenopathy) may be present even though rash is not evident. If such signs and symptoms are present the patient should be evaluated immediately and Lamictal discontinued if an alternative aetiology cannot be established.

Clinical worsening and suicide risk

Suicidal ideation and behaviours (suicidality) have been reported in patients treated with AEDs in several indications, including epilepsy and bipolar disorder. A meta-analysis of placebo-controlled trials of AEDs (including lamotrigine) showed an increased risk of suicidal behaviour (see section 5.1). For AEDs where no such data are available, a similar association with suicide-related events cannot be excluded. Therefore patients should be monitored for signs of suicidality during treatment with Lamictal. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidality emerge.

In patients with bipolar disorder, worsening of depressive symptoms and/or the emergence of suicidality may occur whether or not they are taking medications for bipolar disorder, including Lamictal. Therefore patients receiving Lamictal for bipolar disorder should be closely monitored for clinical worsening (including development of new symptoms) and suicidality, especially at the beginning of a course of treatment, or at the time of dose changes. Certain patients, such as those with a history of suicidal behaviour or thoughts, young adults, and those patients exhibiting a significant degree of suicidal ideation prior to commencement of treatment, may be at a greater risk of suicidal thoughts or suicide attempts, and should receive careful monitoring during treatment.

Consideration should be given to changing the therapeutic regimen, including possibly discontinuing the medication, in patients who experience clinical worsening (including development of new symptoms) and/or the emergence of suicidal ideation/behaviour, especially if these symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

Hormonal contraceptives

Effects of hormonal contraceptives on lamotrigine efficacy
The use of an ethinyloestradiol/levonorgestrel (30 μg/150 μg) combination increases the clearance of lamotrigine by approximately two-fold resulting in decreased lamotrigine levels (see section 4.5). A decrease in lamotrigine levels has been associated with loss of seizure control. Following titration, higher maintenance doses of lamotrigine (by as much as two-fold) will be needed in most cases to attain a maximal therapeutic response. When stopping hormonal contraceptives, the clearance of lamotrigine may be halved. Increases in lamotrigine concentrations may be associated with dose-related adverse events. Patients should be monitored with respect to this.

In women not already taking an inducer of lamotrigine glucuronidation and taking a hormonal contraceptive that includes one week of inactive treatment (for example "pill-free week"), gradual transient increases in lamotrigine levels will occur during the week of inactive treatment (see section 4.2). Variations in lamotrigine levels of this order may be associated with adverse effects. Therefore, consideration should be given to using contraception without a pill-free week, as first-line therapy (for example, continuous hormonal contraceptives or non-hormonal methods).

The interaction between other oral contraceptive or HRT treatments and lamotrigine have not been studied, though they may similarly affect lamotrigine pharmacokinetic parameters.

Effects of lamotrigine on hormonal contraceptive efficacy
An interaction study in 16 healthy volunteers has shown that when lamotrigine and a hormonal contraceptive (ethinyloestradiol/levonorgestrel combination) are administered in combination, there is a modest increase in levonorgestrel clearance and changes in serum FSH and LH (see section 4.5). The impact of these changes on ovarian ovulatory activity is unknown. However, the possibility of these changes resulting in decreased contraceptive efficacy in some patients taking hormonal preparations with lamotrigine cannot be excluded. Therefore patients should be instructed to promptly report changes in their menstrual pattern, i.e. breakthrough bleeding.

Dihydrofolate reductase

Lamotrigine has a slight inhibitory effect on dihydrofolic acid reductase, hence there is a possibility of interference with folate metabolism during long-term therapy (see section 4.6). However, during prolonged human dosing, lamotrigine did not induce significant changes in the haemoglobin concentration, mean corpuscular volume, or serum or red blood cell folate concentrations up to 1 year or red blood cell folate concentrations for up to 5 years.

Renal failure

In single dose studies in subjects with end stage renal failure, plasma concentrations of lamotrigine were not significantly altered. However, accumulation of the glucuronide metabolite is to be expected; caution should therefore be exercised in treating patients with renal failure.

Patients taking other preparations containing lamotrigine

Lamictal should not be administered to patients currently being treated with any other preparation containing lamotrigine without consulting a doctor.

25, 50, 100 and 200 mg tablets:
Excipient of Lamictal tablets

Lamictal tablets contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Development in children

There are no data on the effect of lamotrigine on growth, sexual maturation and cognitive, emotional and behavioural developments in children.

Precautions relating to epilepsy

As with other AEDs, abrupt withdrawal of Lamictal may provoke rebound seizures. Unless safety concerns (for example rash) require an abrupt withdrawal, the dose of Lamictal should be gradually decreased over a period of two weeks.

There are reports in the literature that severe convulsive seizures including status epilepticus may lead to rhabdomyolysis, multiorgan dysfunction and disseminated intravascular coagulation, sometimes with fatal outcome. Similar cases have occurred in association with the use of lamotrigine.

A clinically significant worsening of seizure frequency instead of an improvement may be observed. In patients with more than one seizure type, the observed benefit of control for one seizure type should be weighed against any observed worsening in another seizure type.

Myoclonic seizures may be worsened by lamotrigine.

There is a suggestion in the data that responses in combination with enzyme inducers is less than in combination with non-enzyme inducing antiepileptic agents. The reason is unclear.

In children taking lamotrigine for the treament of typical absence seizures, efficacy may not be maintained in all patients.

Precautions relating to bipolar disorder

Children and adolescents below 18 years
Treatment with antidepressants is associated with an increased risk of suicidal thinking and behaviour in children and adolescents with major depressive disorder and other psychiatric disorders.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

UDP-glucuronyl transferases have been identified as the enzymes responsible for metabolism of lamotrigine. There is no evidence that lamotrigine causes clinically significant induction or inhibition of hepatic oxidative drug-metabolising enzymes, and interactions between lamotrigine and medicinal products metabolised by cytochrome P450 enzymes are unlikely to occur. Lamotrigine may induce its own metabolism but the effect is modest and unlikely to have significant clinical consequences.

Table 6: Effects of other medicinal products on glucuronidation of lamotrigine

Medicinal products that significantly inhibit glucuronidation of lamotrigine	**Medicinal products that significantly induce glucuronidation of lamotrigine**	**Medicinal products that do not significantly inhibit or induce glucuronidation of lamotrigine**
Valproate	Phenytoin	Oxcarbazepine
	Carbamazepine	Felbamate
	Phenobarbitone	Gabapentin
	Primidone	Levetiracetam
	Rifampicin	Pregabalin
	Lopinavir/ritonavir	Topiramate
	Ethinyloestradiol/ levonorgestrel combination*	Zonisamide
		Lithium
		Buproprion
		Olanzapine

* Other oral contraceptive and HRT treatments have not been studied, though they may similarly affect lamotrigine pharmacokinetic parameters (see sections 4.2 and 4.4).

Interactions involving antiepileptic drugs

Valproate, which inhibits the glucuronidation of lamotrigine, reduces the metabolism of lamotrigine and increases the mean half-life of lamotrigine nearly two-fold. In patients receiving concomitant therapy with valproate, the appropriate treatment regimen should be used (see section 4.2).

Certain AEDs (such as phenytoin, carbamazepine, phenobarbitone and primidone) which induce hepatic drug-metabolising enzymes induce the glucuronidation of lamotrigine and enhance the metabolism of lamotrigine. In patients receiving concomitant therapy with phenytoin, carbamazepine, pheonbarbitone or primidone, the appropriate treatment regimen should be used (see section 4.2).

There have been reports of central nervous system events including dizziness, ataxia, diplopia, blurred vision and nausea in patients taking carbamazepine following the introduction of lamotrigine. These events usually resolve when the dose of carbamazepine is reduced. A similar effect was seen during a study of lamotrigine and oxcarbazepine in healthy adult volunteers, but dose reduction was not investigated.

There are reports in the literature of decreased lamotrigine levels when lamotrigine was given in combination with oxcarbazepine. However, in a prospective study in healthy adult volunteers using

doses of 200 mg lamotrigine and 1200 mg oxcarbazepine, oxcarbazepine did not alter the metabolism of lamotrigine and lamotrigine did not alter the metabolism of oxcarbazepine. Therefore in patients receiving concomitant therapy with oxcarbazepine, the treatment regimen for lamotrigine adjunctive therapy without valproate and without inducers of lamotrigine glucuronidation should be used (see section 4.2).

In a study of healthy volunteers, coadministration of felbamate (1200 mg twice daily) with lamotrigine (100 mg twice daily for 10 days) appeared to have no clinically relevant effects on the pharmacokinetics of lamotrigine.

Based on a retrospective analysis of plasma levels in patients who received lamotrigine both with and without gabapentin, gabapentin does not appear to change the apparent clearance of lamotrigine.

Potential interactions between levetiracetam and lamotrigine were assessed by evaluating serum concentrations of both agents during placebo-controlled clinical trials. These data indicate that lamotrigine does not influence the pharmacokinetics of levetiracetam and that levetiracetam does not influence the pharmacokinetics of lamotrigine.

Steady-state trough plasma concentrations of lamotrigine were not affected by concomitant pregabalin (200 mg, 3 times daily) administration. There are no pharmacokinetic interactions between lamotrigine and pregabalin.

Topiramate resulted in no change in plasma concentrations of lamotrigine. Administration of lamotrigine resulted in a 15% increase in topiramate concentrations.

In a study of patients with epilepsy, coadministration of zonisamide (200 to 400 mg/day) with lamotrigine (150 to 500 mg/day) for 35 days had no significant effect on the pharmacokinetics of lamotrigine.

Although changes in the plasma concentrations of other AEDs have been reported, controlled studies have shown no evidence that lamotrigine affects the plasma concentrations of concomitant AEDs. Evidence from *in vitro* studies indicates that lamotrigine does not displace other AEDs from protein binding sites.

Interactions involving other psychoactive agents

The pharmacokinetics of lithium after 2 g of anhydrous lithium gluconate given twice daily for six days to 20 healthy subjects were not altered by co-administration of 100 mg/day lamotrigine.

Multiple oral doses of bupropion had no statistically significant effects on the single dose pharmacokinetics of lamotrigine in 12 subjects and had only a slight increase in the AUC of lamotrigine glucuronide.

In a study in healthy adult volunteers, 15 mg olanzapine reduced the AUC and C_{max} of lamotrigine by an average of 24% and 20%, respectively. An effect of this magnitude is not generally expected to be clinically relevant. Lamotrigine at 200 mg did not affect the pharmacokinetics of olanzapine.

Multiple oral doses of lamotrigine 400 mg daily had no clinically significant effect on the single dose pharmacokinetics of 2 mg risperidone in 14 healthy adult volunteers. Following the co-administration of risperidone 2 mg with lamotrigine, 12 out of the 14 volunteers reported somnolence compared to 1 out of 20 when risperidone was given alone, and none when lamotrigine was administered alone.

In vitro experiments indicated that the formation of lamotrigine's primary metabolite, the 2-N-glucuronide, was minimally inhibited by co-incubation with amitriptyline, bupropion, clonazepam, haloperidol or lorazepam. These experiments also suggested that metabolism of lamotrigine was unlikely to be inhibited by clozapine, fluoxetine, phenelzine, risperidone, sertraline or

trazodone. In addition, a study of bufuralol metabolism using human liver microsome preparations suggested that lamotrigine would not reduce the clearance of medicinal products metabolised predominantly by CYP2D6.

Interactions involving hormonal contraceptives

Effect of hormonal contraceptives on lamotrigine pharmacokinetics
In a study of 16 female volunteers, dosing with 30 µg ethinyloestradiol/150 µg levonorgestrel in a combined oral contraceptive pill caused an approximately two-fold increase in lamotrigine oral clearance, resulting in an average 52% and 39% reduction in lamotrigine AUC and Cmax, respectively. Serum lamotrigine concentrations increased during the course of the week of inactive treatment (including the "pill-free" week), with pre-dose concentrations at the end of the week of inactive treatment being, on average, approximately two-fold higher than during co-therapy (see section 4.4). No adjustments to the recommended dose escalation guidelines for lamotrigine should be necessary solely based on the use of hormonal contraceptives, but the maintenance dose of lamotrigine will need to be increased or decreased in most cases when starting or stopping hormonal contraceptives (see section 4.2).

Effect of lamotrigine on hormonal contraceptive pharmacokinetics
In a study of 16 female volunteers, a steady state dose of 300 mg lamotrigine had no effect on the pharmacokinetics of the ethinyloestradiol component of a combined oral contraceptive pill. A modest increase in oral clearance of the levonorgestrel component was observed, resulting in an average 19% and 12% reduction in levonorgestrel AUC and Cmax, respectively. Measurement of serum FSH, LH and oestradiol during the study indicated some loss of suppression of ovarian hormonal activity in some women, although measurement of serum progesterone indicated that there was no hormonal evidence of ovulation in any of the 16 subjects. The impact of the modest increase in levonorgestrel clearance, and the changes in serum FSH and LH, on ovarian ovulatory activity is unknown (see section 4.4). The effects of doses of lamotrigine other than 300 mg/day have not been studied and studies with other female hormonal preparations have not been conducted.

Interactions involving other medicinal products

In a study in 10 male volunteers, rifampicin increased lamotrigine clearance and decreased lamotrigine half-life due to induction of the hepatic enzymes responsible for glucuronidation. In patients receiving concomitant therapy with rifampicin, the appropriate treatment regimen should be used (see section 4.2).

In a study in healthy volunteers, lopinavir/ritonavir approximately halved the plasma concentrations of lamotrigine, probably by induction of glucuronidation. In patients receiving concomitant therapy with lopinavir/ritonavir, the appropriate treatment regimen should be used (see section 4.2).

4.6 Pregnancy and lactation

Risk related to antiepileptic drugs in general

Specialist advice should be given to women who are of childbearing potential. The need for treatment with AEDs should be reviewed when a woman is planning to become pregnant. In women being treated for epilepsy, sudden discontinuation of AED therapy should be avoided as this may lead to breakthrough seizures that could have serious consequences for the woman and the unborn child.

The risk of congenital malformations is increased by a factor of 2 to 3 in the offspring of mothers treated with AEDs compared with the expected incidence in the general population of approximately 3%. The most frequently reported defects are cleft lip, cardiovascular malformations and neural tube defects. Therapy with multiple AEDs is associated with a higher risk of congenital malformations than monotherapy and therefore monotherapy should be used whenever possible.

Risk related to lamotrigine

Pregnancy
Epidemiological studies involving in total approximately 2000 women exposed to lamotrigine monotherapy during pregnancy cannot exclude an increased risk for congenital malformations. One registry has reported an increased incidence of facial clefts. Other data sets have not confirmed this finding. Animal studies have shown developmental toxicity (see section 5.3).

If therapy with Lamictal is considered necessary during pregnancy, the lowest possible therapeutic dose is recommended.

Lamotrigine has a slight inhibitory effect on dihydrofolic acid reductase and could therefore theoretically lead to an increased risk of embryofoetal damage by reducing folic acid levels (see section 4.4). Intake of folic acid when planning pregnancy and during early pregnancy may be considered.

Physiological changes during pregnancy may affect lamotrigine levels and/or therapeutic effect. There have been reports of decreased lamotrigine plasma levels during pregnancy with a potential risk of loss of seizure control. After birth lamotrigine levels may increase rapidly with a risk of dose-related adverse events. Therefore lamotrigine serum concentrations should be monitored before, during and after pregnancy, as well as shortly after birth. If necessary, the dose should be adapted to maintain the lamotrigine serum concentration at the same level as before pregnancy, or adapted according to clinical response. In addition, dose-related undesirable effects should be monitored after birth.

Lactation
Data indicate that lamotrigine passes into breast milk. In some breast-fed infants, the serum concentrations of lamotrigine reached levels at which pharmacological effects may occur.

The potential benefits of breast-feeding should be weighed against the potential risk of adverse effects occurring in the infant. Should a woman decide to breast-feed while on therapy with lamotrigine, the infant should be monitored for adverse effects.

Fertility
Animal experiments did not reveal impairment of fertility by lamotrigine (see section 5.3).

4.7 Effects on ability to drive and use machines

As there is individual variation in response to all AED therapy, patients taking Lamictal to treat epilepsy should consult their physician on the specific issues of driving and epilepsy.

No studies on the effects on the ability to drive and use machines have been performed. Two volunteer studies have demonstrated that the effect of lamotrigine on fine visual motor co-ordination, eye movements, body sway and subjective sedative effects did not differ from placebo. In clinical trials with lamotrigine adverse reactions of a neurological character such as dizziness and diplopia have been reported. Therefore, patients should see how Lamictal therapy affects them before driving or operating machinery.

4.8 Undesirable effects

The undesirable effects have been divided into epilepsy and bipolar specific sections based on the data currently available. However, both sections should be consulted when considering the overall safety profile of lamotrigine.

The following convention has been utilised for the classification of undesirable effects:- Very common ($\geq$1/10), common ($\geq$1/100, <1/10), uncommon ($\geq$1/1000, <1/100), rare ($\geq$1/10,000, <1/1000), very rare (<1/10,000).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Epilepsy

Blood and lymphatic system disorders

Very rare:	haematological abnormalities including neutropenia, leucopenia, anaemia, thrombocytopenia, pancytopenia, aplastic anaemia, agranulocytosis.

Haematological abnormalities may or may not be associated with the hypersensitivity syndrome (see Immune system disorders**).

Immune system disorders

Very rare:	hypersensitivity syndrome** (including such symptoms as, fever, lymphadenopathy, facial oedema, abnormalities of the blood and liver, disseminated intravascular coagulation, multi-organ failure).

**Rash has also been reported as part of a hypersensitivity syndrome associated with a variable pattern of systemic symptoms including fever, lymphadenopathy, facial oedema and abnormalities of the blood and liver. The syndrome shows a wide spectrum of clinical severity and may, rarely, lead to disseminated intravascular coagulation and multiorgan failure. It is important to note that early manifestations of hypersensitivity (for example fever, lymphadenopathy) may be present even though rash is not evident. If such signs and symptoms are present, the patient should be evaluated immediately and Lamictal discontinued if an alternative aetiology cannot be established.

Psychiatric disorders

Common:	aggression, irritability.
Very rare:	confusion, hallucinations, tics.

Nervous system disorders

During monotherapy clinical trials:

Very common:	headache.
Common:	somnolence, dizziness, tremor, insomnia.
Uncommon:	ataxia.
Rare:	nystagmus.

During other clinical experience:

Very common:	somnolence, ataxia, dizziness, headache.
Common:	nystagmus, tremor, insomnia.
Very rare:	agitation, unsteadiness, movement disorders, worsening of Parkinson's disease, extrapyramidal effects, choreoathetosis, increase in seizure frequency.

There have been reports that lamotrigine may worsen parkinsonian symptoms in patients with pre-existing Parkinson’s disease, and isolated reports of extrapyramidal effects and choreoathetosis in patients without this underlying condition.

Eye disorders

During monotherapy clinical trials:

Uncommon:	diplopia, blurred vision.

During other clinical experience:

Very common:	diplopia, blurred vision.
Rare:	conjunctivitis.

Gastrointestinal disorders

During monotherapy clinical trials:

Common: nausea, vomiting, diarrhoea.

During other clinical experience:
Very common: nausea, vomiting.
Common: diarrhoea.

Hepato-biliary disorders
Very rare: hepatic failure, hepatic dysfunction, increased liver function tests.

Hepatic dysfunction usually occurs in association with hypersensitivity reactions but isolated cases have been reported without overt signs of hypersensitivity.

Skin and subcutaneous tissue disorders
Very common: skin rash.
Rare: Stevens–Johnson Syndrome.
Very rare: toxic epidermal necrolysis.

In double-blind, adjunctive clinical trials in adults, skin rashes occurred in up to 10% of patients taking lamotrigine and in 5% of patients taking placebo. The skin rashes led to the withdrawal of lamotrigine treatment in 2% of patients. The rash, usually maculopapular in appearance, generally appears within eight weeks of starting treatment and resolves on withdrawal of Lamictal (see section 4.4).

Serious potentially life-threatening skin rashes, including Stevens–Johnson syndrome and toxic epidermal necrolysis (Lyell's Syndrome) have been reported. Although the majority recover on withdrawal of lamotrigine treatment, some patients experience irreversible scarring and there have been rare cases of associated death (see section 4.4).

The overall risk of rash, appears to be strongly associated with:

- high initial doses of lamotrigine and exceeding the recommended dose escalation of lamotrigine therapy (see section 4.2)
- concomitant use of valproate (see section 4.2).

Rash has also been reported as part of a hypersensitivity syndrome associated with a variable pattern of systemic symptoms (see Immune system disorders**).

Musculoskeletal and connective tissue disorders
Very rare: lupus-like reactions.

General disorders and administration site conditions
Common: tiredness.

Bipolar Disorder

The undesirable effects below should be considered alongside those seen in epilepsy for an overall safety profile of lamotrigine.

Nervous system disorders
During bipolar disorder clinical trials:
Very common: headache.
Common: agitation, somnolence, dizziness.

Gastrointestinal disorders
During bipolar disorder clinical trials:
Common: dry mouth

Skin and subcutaneous tissue disorders
During bipolar disorder clinical trials:
Very common: skin rash.
Rare: Stevens–Johnson Syndrome.

When all bipolar disorder studies (controlled and uncontrolled) conducted with lamotrigine are considered, skin rashes occurred in 12% of patients on lamotrigine. Whereas, in controlled clinical trials with bipolar disorder patients, skin rashes occurred in 8% of patients taking lamotrigine and in 6% of patients taking placebo.

Musculoskeletal and connective tissue disorders
During bipolar disorder clinical trials:
Common: arthralgia.

General disorders and administration site conditions
During bipolar disorder clinical trials:
Common: pain, back pain.

4.9 Overdose

Symptoms and signs

Acute ingestion of doses in excess of 10 to 20 times the maximum therapeutic dose has been reported. Overdose has resulted in symptoms including nystagmus, ataxia, impaired consciousness and coma.

Treatment

In the event of overdosage, the patient should be admitted to hospital and given appropriate supportive therapy. Therapy aimed at decreasing absorption (activated charcoal, laxative or gastric lavage) should be performed if indicated. There is no experience with haemodialysis as treatment of overdose. In six volunteers with kidney failure, 20% of the lamotrigine was removed from the body during a 4-hour haemodialysis session (see section 5.2).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: other antiepileptics, ATC code: N03AX09.

Mechanism of action

The results of pharmacological studies suggest that lamotrigine is a use- and voltage-dependent blocker of voltage gated sodium channels. It inhibits sustained repetitive firing of neurones and inhibits release of glutamate (the neurotransmitter which plays a key role in the generation of epileptic seizures). These effects are likely to contribute to the anticonvulsant properties of lamotrigine.

In contrast, the mechanisms by which lamotrigine exerts its therapeutic action in bipolar disorder have not been established, although interaction with voltage gated sodium channels is likely to be important.

Pharmacodynamic effects

In tests designed to evaluate the central nervous system effects of medicinal products, the results obtained using doses of 240 mg lamotrigine administered to healthy volunteers did not differ from

placebo, whereas both 1000 mg phenytoin and 10 mg diazepam each significantly impaired fine visual motor co-ordination and eye movements, increased body sway and produced subjective sedative effects.

In another study, single oral doses of 600 mg carbamazepine significantly impaired fine visual motor co-ordination and eye movements, while increasing both body sway and heart rate, whereas results with lamotrigine at doses of 150 mg and 300 mg did not differ from placebo.

Clinical efficacy and safety in children aged 1 to 24 months

The efficacy and safety of adjunctive therapy in partial seizures in patients aged 1 to 24 months has been evaluated in a small double-blind placebo-controlled withdrawal study. Treatment was initiated in 177 subjects, with a dose titration schedule similar to that of children aged 2 to 12 years. Lamotrigine 2 mg tablets are the lowest strength available, therefore the standard dosing schedule was adapted in some cases during the titration phase (for example, by administering a 2 mg tablet on alternate days when the calculated dose was less than 2 mg). Serum levels were measured at the end of week 2 of titration and the subsequent dose either reduced or not increased if the concentration exceeded 0.41 µg/mL, the expected concentration in adults at this time point. Dose reductions of up to 90% were required in some patients at the end of week 2. Thirty-eight responders (> 40% decrease in seizure frequency) were randomised to placebo or continuation of lamotrigine. The proportion of subjects with treatment failure was 84% (16/19 subjects) in the placebo arm and 58% (11/19 subjects) in the lamotrigine arm. The difference was not statistically significant: 26.3%, CI95% -2.6% <> 50.2%, p=0.07.

A total of 256 subjects between 1 to 24 months of age have been exposed to lamotrigine in the dose range 1 to 15 mg/kg/day for up to 72 weeks. The safety profile of lamotrigine in children aged 1 month to 2 years was similar to that in older children except that clinically significant worsening of seizures (>=50%) was reported more often in children under 2 years of age (26%) as compared to older children (14%).

Clinical efficacy and safety in Lennox-Gastaut syndrome

There are no data for monotherapy in seizures associated with Lennox-Gastaut syndrome.

Clinical efficacy in the prevention of mood episodes in patients with bipolar disorder

The efficacy of lamotrigine in the prevention of mood episodes in patients with bipolar I disorder has been evaluated in two studies.

Study SCAB2003 was a multicentre, double-blind, double dummy, placebo and lithium-controlled, randomised fixed dose evaluation of the long-term prevention of relapse and recurrence of depression and/or mania in patients with bipolar I disorder who had recently or were currently experiencing a major depressive episode. Once stabilised using lamotrigine monotherapy or adjunctive therapy, patients were randomly assigned into one of five treatment groups: lamotrigine (50, 200, 400 mg/day), lithium (serum levels of 0.8 to 1.1 mMol/L) or placebo for a maximum of 76 weeks (18 months). The primary endpoint was "Time to Intervention for a Mood Episode (TIME)", where the interventions were additional pharmacotherapy or electroconvulsive therapy (ECT). Study SCAB2006 had a similar design as study SCAB2003, but differed from study SCAB2003 in evaluating a flexible dose of lamotrigine (100 to 400 mg/day) and including patients with bipolar I disorder who had recently or were currently experiencing a manic episode. The results are shown in Table 7.

Table 7: Summary of results from studies investigating the efficacy of lamotrigine in the prevention of mood episodes in patients with bipolar I disorder

'Proportion' of patients being event free at week 76						
	Study SCAB2003 Bipolar I			**Study SCAB2006 Bipolar I**		
Inclusion criterion	Major depressive episode			Major manic episode		
	Lamotrigine	Lithium	Placebo	Lamotrigine	Lithium	Placebo
Intervention free	0.22	0.21	0.12	0.17	0.24	0.04
p-value Log rank test	0.004	0.006	-	0.023	0.006	-
Depression free	0.51	0.46	0.41	0.82	0.71	0.40
p-value Log rank test	0.047	0.209	-	0.015	0.167	-
Free of mania	0.70	0.86	0.67	0.53	0.64	0.37
p-value Log rank test	0.339	0.026	-	0.280	0.006	-

In supportive analyses of time to first depressive episode and time to first manic/hypomanic or mixed episode, the lamotrigine-treated patients had significantly longer times to first depressive episode than placebo patients, and the treatment difference with respect to time to manic/hypomanic or mixed episodes was not statistically significant.

The efficacy of lamotrigine in combination with mood stabilisers has not been adequately studied.

Suicidality analysis

The incidence of suicidal ideation and behaviour was evaluated in a pooled analysis of placebo-controlled clinical trials with lamotrigine involving a total of 6467 patients from a number of indications.

In the subset of bipolar disorder trials, the rate of events was numerically, but not statistically significantly, greater for lamotrigine (29/1212 [2.4%]) compared with placebo (19/1054 [1.8%]). In a pooled analysis of psychiatric indications, events were more common in the first month of treatment, in patients taking lamotrigine. Behavioural events were more common in males.

In the subset of epilepsy trials, there were no statistically significant differences in the rate of events between lamotrigine and placebo. Although the number of suicidal ideation and behaviour events was too low (6/1073 [0.6%] on lamotrigine and 2/805 [0.3%] on placebo) to allow a definitive comparison between treatment groups, the relative rate reported from this lamotrigine analysis is consistent with the reported class effect for AEDs (see section 4.4).

Study of the effect of lamotrigine on cardiac conduction

A study in healthy adult volunteers evaluated the effect of repeat doses of lamotrigine (up to 400 mg/day) on cardiac conduction, as assessed by 12-lead ECG. There was no clinically significant effect of lamotrigine on QT interval compared to placebo.

5.2 Pharmacokinetic properties

Absorption

Lamotrigine is rapidly and completely absorbed from the gut with no significant first-pass metabolism. Peak plasma concentrations occur approximately 2.5 hours after oral administration of lamotrigine. Time to maximum concentration is slightly delayed after food but the extent of absorption is unaffected. There is considerable inter-individual variation in steady state maximum concentrations but within an individual, concentrations rarely vary.

Distribution

Binding to plasma proteins is about 55%; it is very unlikely that displacement from plasma proteins would result in toxicity.

The volume of distribution is 0.92 to 1.22 L/kg.

Metabolism

UDP-glucuronyl transferases have been identified as the enzymes responsible for metabolism of lamotrigine.

Lamotrigine induces its own metabolism to a modest extent depending on dose. However, there is no evidence that lamotrigine affects the pharmacokinetics of other AEDs and data suggest that interactions between lamotrigine and medicinal products metabolised by cytochrome P_{450} enzymes are unlikely to occur.

Elimination

The apparent plasma clearance in healthy subjects is approximately 30 mL/min. Clearance of lamotrigine is primarily metabolic with subsequent elimination of glucuronide-conjugated material in urine. Less than 10% is excreted unchanged in the urine. Only about 2% of lamotrigine-related material is excreted in faeces. Clearance and half-life are independent of dose. The apparent plasma half-life in healthy subjects is estimated to be approximately 33 hours (range 14 to 103 hours). In a study of subjects with Gilbert's Syndrome, mean apparent clearance was reduced by 32% compared with normal controls but the values are within the range for the general population.

The half-life of lamotrigine is greatly affected by concomitant medicinal products. Mean half-life is reduced to approximately 14 hours when given with glucuronidation-inducing medicinal products such as carbamazepine and phenytoin and is increased to a mean of approximately 70 hours when co-administered with valproate alone (see section 4.2).

Linearity

The pharmacokinetics of lamotrigine are linear up to 450 mg, the highest single dose tested.

Special patient populations

Children
Clearance adjusted for body weight is higher in children than in adults with the highest values in children under five years. The half-life of lamotrigine is generally shorter in children than in adults with a mean value of approximately 7 hours when given with enzyme-inducing medicinal products such as carbamazepine and phenytoin and increasing to mean values of 45 to 50 hours when co-administered with valproate alone (see section 4.2).

Infants aged 2 to 26 months
In 143 paediatric patients aged 2 to 26 months, weighing 3 to 16 kg, clearance was reduced compared to older children with the same body weight, receiving similar oral doses per kg body weight as children older than 2 years. The mean half-life was estimated at 23 hours in infants younger than 26 months on enzyme-inducing therapy, 136 hours when co-administered with valproate and 38 hours in subjects treated without enzyme inducers/inhibitors. The inter-individual variability for oral clearance was high in the group of paediatric patients of 2 to 26 months (47%). The predicted serum concentration levels in children of 2 to 26 months were in general in the same range as those in older children, though higher Cmax levels are likely to be observed in some children with a body weight below 10 kg.

Elderly
Results of a population pharmacokinetic analysis including both young and elderly patients with epilepsy, enrolled in the same trials, indicated that the clearance of lamotrigine did not change to a clinically relevant extent. After single doses apparent clearance decreased by 12% from 35 mL/min at age 20 to 31 mL/min at 70 years. The decrease after 48 weeks of treatment was 10% from 41 to 37 mL/min between the young and elderly groups. In addition, pharmacokinetics of lamotrigine was studied in 12 healthy elderly subjects following a 150 mg single dose. The mean clearance in the elderly (0.39 mL/min/kg) lies within the range of the mean clearance values (0.31 to 0.65 mL/min/kg) obtained in nine studies with non-elderly adults after single doses of 30 to 450 mg.

Renal impairment
Twelve volunteers with chronic renal failure, and another six individuals undergoing hemodialysis were each given a single 100 mg dose of lamotrigine. Mean clearances were 0.42 mL/min/kg (chronic renal failure), 0.33 mL/min/kg (between hemodialysis) and 1.57 mL/min/kg (during hemodialysis), compared with 0.58 mL/min/kg in healthy volunteers. Mean plasma half-lives were 42.9 hours (chronic renal failure), 57.4 hours (between hemodialysis) and 13.0 hours (during hemodialysis), compared with 26.2 hours in healthy volunteers. On average, approximately 20% (range = 5.6 to 35.1) of the amount of lamotrigine present in the body was eliminated during a 4-hour hemodialysis session. For this patient population, initial doses of lamotrigine should be based on the patient's concomitant medicinal products; reduced maintenance doses may be effective for patients with significant renal functional impairment (see sections 4.2 and 4.4).

Hepatic impairment
A single dose pharmacokinetic study was performed in 24 subjects with various degrees of hepatic impairment and 12 healthy subjects as controls. The median apparent clearance of lamotrigine was 0.31, 0.24 or 0.10 mL/min/kg in patients with Grade A, B, or C (Child-Pugh Classification) hepatic impairment, respectively, compared with 0.34 mL/min/kg in the healthy controls. Initial, escalation and maintenance doses should generally be reduced in patients with moderate or severe hepatic impairment (see section 4.2).

5.3 Preclinical safety data

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

In reproductive and developmental toxicity studies in rodents and rabbits, no teratogenic effects but reduced foetal weight and retarded skeletal ossification were observed, at exposure levels below or similar to the expected clinical exposure. Since higher exposure levels could not be tested in animals due to the severity of maternal toxicity, the teratogenic potential of lamotrigine has not been characterised above clinical exposure.

In rats, enhanced foetal as well as post-natal mortality was observed when lamotrigine was administered during late gestation and through the early post-natal period. These effects were observed at the expected clinical exposure.

In juvenile rats, an effect on learning in the Biel maze test, a slight delay in balanopreputial separation and vaginal patency and a decreased postnatal body weight gain in F1 animals were observed at exposures approximately two-times higher than the therapeutic exposures in human adults.

Animal experiments did not reveal impairment of fertility by lamotrigine. Lamotrigine reduced foetal folic acid levels in rats. Folic acid deficiency is assumed to be associated with an enhanced risk of congenital malformations in animals as well as in humans.

Lamotrigine caused a dose-related inhibition of the hERG channel tail current in human embryonic kidney cells. The IC50 was approximately nine-times above the maximum therapeutic free concentration. Lamotrigine did not cause QT prolongation in animals at exposures up to approximately two-times the maximum therapeutic free concentration. In a clinical study, there was no clinically significant effect of lamotrigine on QT interval in healthy adult volunteers (see section 5.1).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

25, 50, 100 and 200 mg tablets:
Lactose monohydrate
Microcrystalline cellulose
Povidone K30
Sodium starch glycolate (Type A)
Iron oxide yellow (E172)
Magnesium stearate.

2, 5, 25, 50, 100 and 200 mg dispersible/chewable tablets:
Calcium carbonate
Low-substituted hydroxypropyl cellulose
Aluminium magnesium silicate
Sodium starch glycolate (Type A)
Povidone K30
Saccharin sodium
Magnesium stearate
Blackcurrant flavour.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

25, 50, 100 and 200 mg tablets, 5, 25, 50, 100 and 200 mg dispersible/chewable tablets:
Three years.

2 mg dispersible/chewable tablets:
Two years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

25 mg tablets:
PVC/aluminium foil blister.

Packs of 14, 21, 30, 42, 50, 56 or 100 tablets.
Starter pack of 21 or 42 tablets.

50 mg tablets:
PVC/aluminium foil blister.

Packs of 14, 30, 42, 56, 90 or 100 tablets.
Starter pack of 42 tablets.

100 mg tablets:
PVC/aluminium foil blister.

Packs of 30, 50, 56, 60, 90 or 100 tablets.

200 mg tablets:
PVC/aluminium foil blister.

Packs of 30, 56 or 100 tablets.

2 mg dispersible/chewable tablets:
HDPE bottles with a child resistant/tamper evident closure.

Packs of 30 dispersible/chewable tablets.

5 mg dispersible/chewable tablets:
PVC/PVdC/aluminium foil blister.

Packs of 10, 14, 28, 30, 50 or 56 dispersible/chewable tablets.

25 mg dispersible/chewable tablets:
PVC/PVdC/aluminium foil blister.

Packs of 10, 14, 21, 28, 30, 42, 50, 56 or 60 dispersible/chewable tablets.
Starter pack of 21 or 42 dispersible/chewable tablets.

50 mg dispersible/chewable tablets:
PVC/PVdC/aluminium foil blister.

Packs of 10, 14, 30, 42, 50, 56, 60, 90, 100 or 200 dispersible/chewable tablets.
Starter pack of 42 dispersible/chewable tablets.

100 mg dispersible/chewable tablets:
PVC/PVdC/aluminium foil blister.

Packs of 10, 30, 50, 56, 60, 90, 100 or 200 dispersible/chewable tablets.

200 mg dispersible/chewable tablets:
PVC/PVdC/aluminium foil blister.

Packs of 10, 30, 50, 56, 60, 90, 100 or 200 dispersible/chewable tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

{DD month YYYY}

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

{MM/YYYY}

[To be completed nationally]

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 25 mg tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 25 mg lamotrigine

3. LIST OF EXCIPIENTS

Contains lactose monohydrate – see package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

14 tablets
21 tablets
30 tablets
42 tablets
50 tablets
56 tablets
100 tablets
Starter pack 21 tablets, valproate add-on therapy
Starter pack 42 tablets, monotherapy

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Do not chew or crush
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 25 mg tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

(Starter pack 21 tablets, valproate add-on therapy – calender pack showing day numbers):
1 3 5 7 9 11 13 (one pocket)
2 4 6 8 10 12 14 (no pocket)
15 17 19 21 23 25 27 (one pocket)
16 18 20 22 24 26 28 (one pocket)

(Starter pack 42 tablets, monotherapy – calender pack showing day numbers):
1 2 3 4 5 6 7 (one pocket)
8 9 10 11 12 13 14 (one pocket)
15 16 17 18 19 20 21 (two pockets)
22 23 24 25 26 27 28 (two pockets)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 50 mg tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 50 mg lamotrigine

3. LIST OF EXCIPIENTS

Contains lactose monohydrate – see package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

14 tablets
30 tablets
42 tablets
56 tablets
90 tablets
100 tablets
Starter pack 42 tablets, non-valproate add-on therapy

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Do not chew or crush
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 50 mg tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

(Starter pack 42 tablets, non-valproate add-on therapy – calender pack showing day numbers):
1 2 3 4 5 6 7 (1 pocket)
8 9 10 11 12 13 14 (1 pocket)
15 16 17 18 19 20 21 (2 pockets)
22 23 24 25 26 27 28 (2 pockets)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 100 mg tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 100 mg lamotrigine

3. LIST OF EXCIPIENTS

Contains lactose monohydrate – see package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

30 tablets
50 tablets
56 tablets
60 tablets
90 tablets
100 tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Do not chew or crush
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 100 mg tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 200 mg tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each tablet contains 200 mg lamotrigine

3. LIST OF EXCIPIENTS

Contains lactose monohydrate – see package leaflet for further information

4. PHARMACEUTICAL FORM AND CONTENTS

30 tablets
56 tablets
100 tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Do not chew or crush
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 200 mg tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

BOTTLE

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 2 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each dispersible/chewable tablet contains 2 mg lamotrigine

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

30 dispersible/chewable tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 5 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each dispersible/chewable tablet contains 5 mg lamotrigine

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

10 dispersible/chewable tablets
14 dispersible/chewable tablets
28 dispersible/chewable tablets
30 dispersible/chewable tablets
50 dispersible/chewable tablets
56 dispersible/chewable tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 5 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 25 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each dispersible/chewable tablet contains 25 mg lamotrigine

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

10 dispersible/chewable tablets
14 dispersible/chewable tablets
21 dispersible/chewable tablets
28 dispersible/chewable tablets
30 dispersible/chewable tablets
42 dispersible/chewable tablets
50 dispersible/chewable tablets
56 dispersible/chewable tablets
60 dispersible/chewable tablets
Starter pack 21 dispersible/chewable tablets, valproate add-on therapy
Starter pack 42 dispersible/chewable tablets, monotherapy

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 25 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

(Starter pack 21 tablets, valproate add-on therapy – calender pack showing day numbers):
1 3 5 7 9 11 13 (one pocket)
2 4 6 8 10 12 14 (no pocket)
15 17 19 21 23 25 27 (one pocket)
16 18 20 22 24 26 28 (one pocket)

(Starter pack 42 tablets, monotherapy – calender pack showing day numbers):
1 2 3 4 5 6 7 (one pocket)
8 9 10 11 12 13 14 (one pocket)
15 16 17 18 19 20 21 (two pockets)
22 23 24 25 26 27 28 (two pockets)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 50 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each dispersible/chewable tablet contains 50 mg lamotrigine

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

10 dispersible/chewable tablets
14 dispersible/chewable tablets
30 dispersible/chewable tablets
42 dispersible/chewable tablets
50 dispersible/chewable tablets
56 dispersible/chewable tablets
60 dispersible/chewable tablets
90 dispersible/chewable tablets
100 dispersible/chewable tablets
200 dispersible/chewable tablets
Starter pack 42 dispersible/chewable tablets, non-valproate add-on therapy

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 50 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

(Starter pack 42 tablets, non-valproate add-on therapy – calender pack showing day numbers):
1 2 3 4 5 6 7 (1 pocket)
8 9 10 11 12 13 14 (1 pocket)
15 16 17 18 19 20 21 (2 pockets)
22 23 24 25 26 27 28 (2 pockets)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 100 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each dispersible/chewable tablet contains 100 mg lamotrigine

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

10 dispersible/chewable tablets
30 dispersible/chewable tablets
50 dispersible/chewable tablets
56 dispersible/chewable tablets
60 dispersible/chewable tablets
90 dispersible/chewable tablets
100 dispersible/chewable tablets
200 dispersible/chewable tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 100 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 200 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. STATEMENT OF ACTIVE SUBSTANCE

Each dispersible/chewable tablet contains 200 mg lamotrigine

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

10 dispersible/chewable tablets
30 dispersible/chewable tablets
50 dispersible/chewable tablets
56 dispersible/chewable tablets
60 dispersible/chewable tablets
90 dispersible/chewable tablets
100 dispersible/chewable tablets
200 dispersible/chewable tablets

5. METHOD AND ROUTE OF ADMINISTRATION

Oral use
Read the package leaflet before use

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP {MM YYYY}

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

[To be completed nationally]

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

[To be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

Lamictal and associated names (see Annex I) 200 mg dispersible/chewable tablets
[See Annex I - To be completed nationally]
Lamotrigine

2. NAME OF THE MARKETING AUTHORISATION HOLDER

[See Annex I - To be completed nationally]

3. EXPIRY DATE

EXP {MM YYYY}

4. BATCH NUMBER

Lot

5. OTHER

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Lamictal and associated names (see Annex I) 25 mg tablets
Lamictal and associated names (see Annex I) 50 mg tablets
Lamictal and associated names (see Annex I) 100 mg tablets
Lamictal and associated names (see Annex I) 200 mg tablets
Lamictal and associated names (see Annex I) 2 mg dispersible/chewable tablets
Lamictal and associated names (see Annex I) 5 mg dispersible/chewable tablets
Lamictal and associated names (see Annex I) 25 mg dispersible/chewable tablets
Lamictal and associated names (see Annex I) 50 mg dispersible/chewable tablets
Lamictal and associated names (see Annex I) 100 mg dispersible/chewable tablets
Lamictal and associated names (see Annex I) 200 mg dispersible/chewable tablets

[See Annex I – To be completed nationally]

lamotrigine

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

In this leaflet

1. WHAT LAMICTAL IS AND WHAT IT IS USED FOR

Lamictal belongs to a group of medicines called *anti-epileptics*. It is used to treat two conditions — **epilepsy** and **bipolar disorder**.

Lamictal treats epilepsy by blocking the signals in the brain that trigger epileptic seizures (fits).
- For adults and children aged 13 years and over, Lamictal can be used on its own or with other medicines, to treat epilepsy. Lamictal can also be used with other medicines to treat the seizures that occur with a condition called Lennox-Gastaut syndrome.
- For children aged between 2 and 12 years, Lamictal can be used with other medicines, to treat those conditions. It can be used on its own to treat a type of epilepsy called typical absence seizures.

Lamictal also treats bipolar disorder.
People with bipolar disorder (sometimes called *manic depression*) have extreme mood swings, with periods of mania (excitement or euphoria) alternating with periods of depression (deep sadness or despair). For adults aged 18 years and over, Lamictal can be used on its own or with other medicines, to prevent the periods of depression that occur in bipolar disorder. It is not yet known how Lamictal works in the brain to have this effect.

2. BEFORE YOU TAKE LAMICTAL

Do not take Lamictal:

- **if you are allergic** *(hypersensitive)* to lamotrigine or any of the other ingredients of Lamictal (listed in Section 6).

If this applies to you:
➔ **Tell your doctor**, and don't take Lamictal.

Take special care with Lamictal
Your doctor needs to know before you take Lamictal:

- **if you have problems with your kidneys**
- **if you have ever developed a rash** when you've taken lamotrigine or other medicines for epilepsy
- **if you are already taking medicine that contains lamotrigine**.

If any of these applies to you:
➔ **Tell your doctor**, who may decide to lower your dose, or that Lamictal is not suitable for you.

Watch out for important symptoms
If you develop any of these symptoms after you start taking Lamictal, **get a doctor's help straight away**:

- **an unusual skin reaction**, such as redness or rashes
- **a sore mouth or eyes**
- **a high temperature** (fever), flu-like symptoms or drowsiness
- **swelling around your face**, or **swollen glands** in your neck, armpit or groin
- **unexpected bleeding or bruising,** or your fingers turning blue
- **a sore throat**, or more infections (such as colds) than usual.

These symptoms are more likely to happen during the first few months of treatment with Lamictal, especially if you start on too high a dose or if your dose is increased too quickly, or if you're taking Lamictal with another medicine called *valproate*. Children are more likely to be affected than adults.

The symptoms listed above can develop into more serious problems, such as organ failure or a very severe skin condition, if they are not treated. If you notice any of these symptoms:
➔ **See a doctor as soon as possible**. Your doctor may decide to carry out tests on your liver, kidneys or blood, and may tell you to stop taking Lamictal.

Thoughts of harming yourself or suicide
People with bipolar disorder can sometimes have thoughts of harming themselves or committing suicide. If you have bipolar disorder, you may be more likely to think like this:

- when you first start treatment
- if you have previously had thoughts about harming yourself or about suicide
- if you are under 25 years old.

Occasionally, people with epilepsy may also have thoughts of harming themselves or committing suicide. A small number of people being treated with Lamictal for bipolar disorder or epilepsy have had these thoughts. If you have distressing thoughts or experiences, or if you notice that you feel worse or develop new symptoms while you're taking Lamictal:
➔ **See a doctor as soon as possible or go to the nearest hospital for help.**

If you're taking Lamictal for epilepsy
The seizures in some types of epilepsy may occasionally become worse or happen more often while you're taking Lamictal. Some patients may experience severe seizures, which may cause serious health problems. If your seizures happen more often, or if you experience a severe seizure while you're taking Lamictal:

➔ **See a doctor as soon as possible**.

Lamictal should not be given to people aged under 18 years to treat bipolar disorder. Medicines to treat depression and other mental health problems increase the risk of suicidal thoughts and behaviour in children and adolescents aged under 18 years.

Taking other medicines
Tell your doctor or pharmacist if you're taking any other medicines, if you've taken any recently, or if you start taking new ones — these include herbal medicines or other medicines you bought without a prescription.

If you are taking certain medicines, your doctor may need to check the dose of Lamictal. These include:

- **oxcarbazepine, felbamate, gabapentin, levetiracetam, pregabalin, topiramate** or **zonisamide**, used to treat **epilepsy**
- **lithium**, used to treat **mental health problems**
- **bupropion,** used to treat **mental health problems** or to **stop smoking**

➔ **Tell your doctor** if you are taking any of these.

Some medicines interact with Lamictal or make it more likely that you'll have side effects. These include:

- **valproate**, used to treat **epilepsy** and **mental health problems**
- **carbamazepine**, used to treat **epilepsy** and **mental health problems**
- **phenytoin, primidone** or **phenobarbitone**, used to treat **epilepsy**
- **olanzapine**, used to treat **mental health problems**
- **risperidone**, used to treat **mental health problems**
- **rifampicin**, which is an **antibiotic**
- a combination of **lopinavir and ritonavir**, used to treat **Human Immunodeficiency Virus (HIV) infection**
- **hormonal contraceptives**, such as **the Pill** *(see below)*.

➔ **Tell your doctor** if you are taking, or if you start or stop taking, any of these.

Hormonal contraceptives (such as the Pill) can affect the way Lamictal works
Your doctor may recommend that you use a particular type of hormonal contraceptive, or another method of contraception, such as condoms, a cap or a coil. If you are using a hormonal contraceptive like the Pill, your doctor may take samples of your blood to check the level of Lamictal. If you plan to start using a hormonal contraceptive:

➔ **Talk to your doctor,** who will discuss suitable methods of contraception with you.

Lamictal can also affect the way hormonal contraceptives work, although it's unlikely to make them less effective. If you are using a hormonal contraceptive, and you notice any changes in your menstrual pattern, such as breakthrough bleeding or spotting between periods:

➔ **Tell your doctor**. These may be signs that Lamictal is affecting the way your contraceptive is working.

Pregnancy and breast feeding

➔ **Talk to your doctor if you're pregnant, if you might be pregnant, or if you're planning to become pregnant.**

You should not stop treatment for your epilepsy while you're pregnant. However, there is an increased risk of birth defects in babies whose mothers took Lamictal during pregnancy. These defects include cleft lip or cleft palate. Your doctor may advise you to take extra **folic acid** if you're planning to become pregnant and while you're pregnant.
Pregnancy may also alter the effectiveness of Lamictal, so your doctor may take samples of your blood to check the level of Lamictal, and may adjust your dose.

➔ **Talk to your doctor if you're breast feeding or planning to breast feed**. The active ingredient of Lamictal passes into breast milk and may affect your baby. Your doctor will discuss the risks and benefits of breast feeding while you're taking Lamictal, and will check your baby from time to time if you decide to breast feed.

Driving and using machines
Lamictal can cause dizziness and double vision.
➔ **Don't drive or operate machines unless you are sure you're not affected.**

If you have epilepsy, talk to your doctor about driving and using machines.

Tablets:
Important information about some of the ingredients of Lamictal
Lamictal tablets contain small amounts of a sugar called lactose. If you have an intolerance to lactose or any other sugars:
➔ **Tell your doctor,** and don't take Lamictal.

3. HOW TO TAKE LAMICTAL

Always use Lamictal exactly as your doctor has told you to. Check with your doctor or pharmacist if you're not sure.

How much Lamictal to take
It may take a while to find the best dose of Lamictal for you. The dose you take will depend on:
- your age
- whether you are taking Lamictal with other medicines
- whether you have problems with your kidneys or liver.

Your doctor will start you on a low dose, and gradually increase the dose over a few weeks until you reach a dose that works for you (called the *effective dose*). **Never take more Lamictal than your doctor tells you to**.

The usual effective dose of Lamictal for adults and children aged over 12 years is between 100 mg and 400 mg each day.

For children aged 2 to 12 years, the effective dose depends on their body weight — usually, it's between 1 mg and 15 mg for each kilogram of the child's weight, up to a maximum of 400 mg daily.

How to take your dose of Lamictal
Tablets:
Take your dose of Lamictal once or twice a day, as your doctor advises. You can take it with or without food.

Your doctor may also advise you to start or stop taking other medicines, depending on what condition you're being treated for and the way you respond to treatment.
- **Swallow your tablets whole**. Don't break, chew or crush them.
- **Always take the full dose** that your doctor has prescribed. Never take only part of a tablet.

Dispersible/chewable tablets:
Take your dose of Lamictal once or twice a day, as your doctor advises. You can take it with or without food.
- **Always take the full dose** that your doctor has prescribed. Never take only part of a tablet.

Your doctor may also advise you to start or stop taking other medicines, depending on what condition you're being treated for and the way you respond to treatment.

You can take Lamictal dispersible/chewable tablets by swallowing them whole with a little water, by chewing them, or by dissolving them in water:

If you chew the tablet:
You may need to drink a little water at the same time to help the tablet dissolve in your mouth. Then drink some more water to make sure you have swallowed all the medicine.

To make a liquid medicine:

- Put the tablet in a glass with at least enough water to cover the whole tablet.
- Either stir to dissolve, or wait for about a minute, until the tablet is fully dissolved.
- Drink all the liquid.
- Add a little more water to the glass and drink that, to make sure you've taken all the medicine.

If you take more Lamictal than you should
If anyone takes too much Lamictal:
➔ **Contact a doctor or pharmacist immediately**. If possible, show them the Lamictal packet.

Someone who has taken too much Lamictal may have any of these symptoms:

- rapid, uncontrollable eye movements *(nystagmus)*
- clumsiness and lack of co-ordination, affecting their balance *(ataxia)*
- loss of consciousness or coma.

If you forget to take Lamictal
Don't take extra tablets or a double dose to make up for a forgotten dose.

If you have missed taking a dose of Lamictal:
➔ **Ask your doctor for advice on how to start taking it again**. It's important that you do this.

Don't stop taking Lamictal without advice
Take Lamictal for as long as your doctor recommends. Don't stop unless your doctor advises you to.

If you are taking Lamictal for epilepsy
To stop taking Lamictal, **it is important that your dose is reduced gradually**, over about 2 weeks. If you suddenly stop taking Lamictal, your epilepsy may come back or get worse.

If you are taking Lamictal for bipolar disorder
Lamictal may take some time to work, so you are unlikely to feel better straight away. If you stop taking Lamictal, your dose will not need to be reduced gradually. But you should still talk to your doctor first, if you want to stop taking Lamictal.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Lamictal can cause side effects, but not everyone gets them.

Allergic reaction or potentially serious skin reaction: get a doctor's help straight away
A small number of people taking Lamictal get an allergic reaction or potentially serious skin reaction, which may develop into more serious, and even life-threatening, problems if they are not treated. Symptoms of these reactions include:

- **skin rashes or redness**
- **a sore mouth or eyes**
- **a high temperature** (fever), flu-like symptoms or drowsiness

- **swelling around your face**, or **swollen glands** in your neck, armpit or groin
- **unexpected bleeding or bruising**, or your fingers turning blue
- **a sore throat**, or more infections (such as colds) than usual.

In many cases, these symptoms will be signs of less serious side effects. **But you must be aware that they are potentially serious** — so, if you notice any of these symptoms:

➔ **See a doctor** as **soon as possible**. Your doctor may decide to carry out tests on your liver, kidneys or blood, and may tell you to stop taking Lamictal.

Very common side effects
These may affect **more than 1 in 10** people:
- headache
- feeling dizzy
- feeling sleepy or drowsy
- clumsiness and lack of co-ordination *(ataxia)*
- double vision or blurred vision
- feeling sick *(nausea)* or being sick *(vomiting)*
- skin rash.

Common side effects
These may affect **up to 1 in 10** people:
- aggression or irritability
- rapid, uncontrollable eye movements *(nystagmus)*
- shaking or tremors
- difficulty in sleeping
- diarrhoea
- dry mouth
- feeling tired
- pain in your back or joints, or elsewhere.

Rare side effects
These may affect **up to 1 in 1,000** people:
- itchy eyes, with discharge and crusty eyelids *(conjunctivitis)*
- a rare skin condition, with severe blisters, and bleeding from the lips, eyes, mouth, nose and genital area *(Stevens–Johnson syndrome)*.

Very rare side effects
These may affect **up to 1 in 10,000** people:
- hallucinations ('seeing' or 'hearing' things that aren't really there)
- confusion or agitation
- feeling 'wobbly' or unsteady when you move about
- uncontrollable body movements *(tics)*, uncontrollable muscle spasms affecting the eyes, head and torso *(choreoathetosis)*, or other unusual body movements such as jerking, shaking or stiffness
- a severe skin reaction, starting with a painful red area, developing into large blisters then peeling of layers of skin *(toxic epidermal necrolysis)*
- in people who already have epilepsy, seizures happening more often
- changes in liver function, which will show up in blood tests, or liver failure
- changes which may show up in blood tests — including reduced numbers of red blood cells *(anaemia)*, reduced numbers of white blood cells *(leucopenia, neutropenia, agranulo-cytosis)*, reduced numbers of platelets *(thrombocytopenia)*, reduced numbers of all these types of cell *(pancytopenia),* and a disorder of the bone marrow called *aplastic anaemia*
- a disorder of blood clotting, which can cause unexpected bleeding or bruising *(disseminated intravascular coagulation)*

- a high temperature (*fever*)
- swelling around the face (*oedema*) or swollen glands in the neck, armpit or groin (*lymphadenopathy*)
- in people who already have Parkinson's disease, worsening of the symptoms.

If you get side effects

➔ If any of the side effects becomes severe or troublesome, or if you notice any side effects not listed in this leaflet **please tell your doctor or pharmacist**.

5. HOW TO STORE LAMICTAL

Keep Lamictal out of the sight and reach of children.

Do not use Lamictal after the expiry date shown on the blisters, carton or bottle. The expiry date refers to the last day of that month.

Lamictal does not require any special storage conditions.

If you have any unwanted Lamictal tablets, don't dispose of them in your waste water or your household rubbish. Take them back to your pharmacist, who will dispose of them in a way that won't harm the environment.

6. FURTHER INFORMATION

What Lamictal tablets contain

The active substance is lamotrigine. Each tablet contains 25 mg, 50 mg, 100 mg or 200 mg lamotrigine.
The other ingredients are: lactose monohydrate, microcrystalline cellulose, povidone K30, sodium starch glycolate (Type A), iron oxide yellow (E172) and magnesium stearate.

What Lamictal dispersible/chewable tablets contain

The active substance is lamotrigine. Each dispersible/chewable tablet contains 2 mg, 5 mg, 25 mg, 50 mg, 100 mg or 200 mg lamotrigine.
The other ingredients are: calcium carbonate, low substituted hydroxypropyl cellulose, aluminium magnesium silicate, sodium starch glycolate (Type A), povidone K30, saccharin sodium, magnesium stearate, blackcurrant flavour.

What Lamictal tablets look like and contents of the pack

Lamictal tablets (all strengths) are square with rounded corners, and pale, yellowish brown in colour. Not all listed pack sizes may be available in your country.

Lamictal 25 mg tablets are marked 'GSEC7' on one side and '25' on the other. Each pack contains blisters of 14, 21, 30, 42, 50, 56 or 100 tablets. Starter packs containing 21 or 42 tablets are also available for use during the first few weeks of treatment when the dose is being slowly increased.

Lamictal 50 mg tablets are marked 'GSEE1' on one side and '50' on the other. Each pack contains blisters of 14, 30, 42, 56, 90 or 100 tablets. Starter packs containing 42 tablets are also available for use during the first few weeks of treatment when the dose is being slowly increased.

Lamictal 100 mg tablets are marked 'GSEE5' on one side and '100' on the other. Each pack contains blisters of 30, 50, 56, 60, 90 or 100 tablets.

Lamictal 200 mg tablets are marked 'GSEE7' on one side and '200' on the other. Each pack contains blisters of 30, 56 or 100 tablets.

What Lamictal dispersible/chewable tablets look like and contents of the pack
Lamictal dispersible/chewable tablets (all strengths) are white to off-white, and may be slightly mottled. They smell of blackcurrant. Not all listed pack sizes may be available in your country.

Lamictal 2 mg dispersible/chewable tablets are round. They are marked 'LTG' above the number '2' on one side; and with two ovals overlapping at right angles on the other. Each bottle contains 30 tablets.

Lamictal 5 mg dispersible/chewable tablets are elongated with curved sides. They are marked 'GS CL2' on one side; and '5' on the other. Each pack contains blisters of 10, 14, 28, 30, 50 or 56 tablets.

Lamictal 25 mg dispersible/chewable tablets are square with rounded corners. They are marked 'GSCL5' on one side; and '25' on the other. Each pack contains blisters of 10, 14, 21, 28, 30, 42, 50, 56 or 60 tablets. Starter packs containing 21 or 42 tablets are available for use during the first few weeks of treatment when the dose is being slowly increased.

Lamictal 50 mg dispersible/chewable tablets are square with rounded corners. They are marked 'GSCX7' on one side; and '50' on the other. Each pack contains blisters of 10, 14, 30, 42, 50, 56, 60, 90, 100 or 200 tablets. Starter packs containing 42 tablets are available for use during the first few weeks of treatment when the dose is being slowly increased.

Lamictal 100 mg dispersible/chewable tablets are square with rounded corners. They are marked 'GSCL7' on one side; and '100' on the other. Each pack contains blisters of 10, 30, 50, 56, 60, 90, 100 or 200 tablets.

Lamictal 200 mg dispersible/chewable tablets are square with rounded corners. They are marked 'GSEC5' on one side; and '200' on the other. Each pack contains blisters of 10, 30, 50, 56, 60, 90, 100 or 200 tablets.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder: [See Annex I - To be completed nationally]

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

Manufacturer: <Glaxo Operations UK Limited (Trading as Glaxo Wellcome Operations), Priory Street, Ware, Hertfordshire SG12 0DJ, United Kingdom.>

<GlaxoSmithKline Pharmaceuticals S.A., Ul. Grunwaldzka 189, 60-322 Poznan, Poland.>

<Glaxo Wellcome GmbH & Co., Industriestrasse 32-36, 23843 Bad Oldesloe, Germany.>

<GlaxoSmithKline EOOD, Gradinarska Street 5, Sofia 1510, Bulgaria.>

<Glaxo Wellcome S.A., Avda. Extremadura, 3, Poligono Industrial Allenduero, 09400 Aranda de Duero (Burgos), Spain.>

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

[To be completed nationally]

ANNEX IV

CONDITION OF THE MARKETING AUTHORISATION(S)

CONDITIONS CONSIDERED ESSENTIAL FOR THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT INCLUDING PHARMACOVIGILANCE

The Marketing Authorisation Holder commits to timely submission of MR/national variations to implement labelling changes, which may be agreed following Pharmacovigilance Working Party (PhVWP) recommendation concerning suicidal ideation and behaviour with anti-epileptic drugs.