REVISED ANNEX I
LIST OF THE NAMES, PHARMACEUTICAL FORMS, STRENGTHS OF THE MEDICINAL PRODUCTS, ROUTES OF ADMINISTRATION, APPLICANTS, MARKETING AUTHORISATION HOLDERS, PACKAGING AND PACKAGE SIZES IN THE MEMBER STATES

Member State	**Marketing Authorisation Holder (Name, address, phone and fax numbers)**	**Invented Name**	**Strength**	**Pharmaceutical Form**	**Route of administration**	**Packaging**	**Pack Size**
Austria	CSC Pharmaceuticals Handels-GmbH, Heiligenstädter Strasse 395B - A-1190 Wien Phone +43-2243-30010-12/ Fax +43-22 62 60 66 00	Aulin	3 %	Gel	Cutaneous use	Tube	30g,50g,100g, 15g
Austria	CSC Pharmaceuticals Handels-GmbH, Heiligenstädter Strasse 395B - A-1190 Wien Phone +43-2243-30010-12/ Fax +43-22 62 60 66 00	Aulin	100 mg	Granules	Oral use	Sachet	15, 30
Austria	CSC Pharmaceuticals Handels-GmbH, Heiligenstädter Strasse 395B - A-1190 Wien Phone +43-2243-30010-12/ Fax +43-22 62 60 66 00	Aulin	100 mg	Suppository	Rectal use	Strip	5, 10
Austria	CSC Pharmaceuticals Handels-GmbH, Heiligenstädter Strasse 395B - A-1190 Wien Phone +43-2243-30010-12/ Fax +43-22 62 60 66 00	Aulin	200 mg	Suppository	Rectal use	Strip	5, 10
Austria	CSC Pharmaceuticals Handels-GmbH, Heiligenstädter Strasse 395B - A-1190 Wien Phone +43-2243-30010-12/ Fax +43-22 62 60 66 00	Aulin	100 mg	Tablet	Oral use	Blister	6, 15, 30, 60
Austria	CSC Pharmaceuticals Handels-GmbH, Heiligenstädter Strasse 395B - A-1190 Wien Phone +43-2243-30010-12/ Fax +43-22 62 60 66 00	Mesulid	100 mg	Granules	Oral use	Sachet	15, 30
Austria	CSC Pharmaceuticals Handels-GmbH, Heiligenstädter Strasse 395B - A-1190 Wien Phone +43-2243-30010-12/ Fax +43-22 62 60 66 00	Mesulid	100 mg	Suppository	Rectal use	Strip	5, 10
Austria	CSC Pharmaceuticals Handels-GmbH, Heiligenstädter Strasse 395B - A-1190 Wien Phone +43-2243-30010-12/ Fax +43-22 62 60 66 00	Mesulid	200 mg	Suppository	Rectal use	Strip	5, 10
Austria	CSC Pharmaceuticals Handels-GmbH, Heiligenstädter Strasse 395B - A-1190 Wien Phone +43-2243-30010-12/ Fax +43-22 62 60 66 00	Mesulid	100 mg	Tablet	Oral use	Blister	15, 30, 60

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Belgium	Therabel Pharma s.a. Rue Egide Van Ophem 108 - B-1180 Brussels Belgium Tel.: 00 32 2 370 46 00 - Fax.: 00 32 2 370 46 90	AULIN	100 mg	Tablet	Oral use	Blister	14 – 30 – 60 U.D. 30 – 60
Belgium	Therabel Pharma s.a. Rue Egide Van Ophem 108 - B-1180 Brussels Belgium Tel.: 00 32 2 370 46 00 - Fax.: 00 32 2 370 46 90	AULIN	100 mg	Granules for oral suspension	Oral use	Sachet	14 – 30 – 60
Belgium	Therabel Pharma s.a. Rue Egide Van Ophem 108 - B-1180 Brussels Belgium Tel.: 00 32 2 370 46 00 - Fax.: 00 32 2 370 46 90	MESULID	100 mg	Tablet	Oral use	Blister	14 – 30 – 60 U.D. 30 – 60
Belgium	Therabel Pharma s.a. Rue Egide Van Ophem 108 - B-1180 Brussels Belgium Tel.: 00 32 2 370 46 00 - Fax.: 00 32 2 370 46 90	MESULID	100 mg	Granules for oral suspension	Oral use	Sachet	14 – 30 – 60
Belgium	Therabel Pharma s.a. Rue Egide Van Ophem 108 - B-1180 Brussels Belgium Tel.: 00 32 2 370 46 00 - Fax.: 00 32 2 370 46 90	MESULID	30 mg/g (3%)	Gel	Cutaneous use	Tube	30 g - 50 g - 100 g
Finland	Aventis Pharma Oy Huopalahdentie 24 - 00350 Finland tel. +358 201 200 300/ tel. +358 201 200 354 Liisa Hurme Fax +358 201 200 495 email: liisa.hurme@aventis.com	Nimed	100 mg	Tablet	Oral use	Blister	10, 30, 50, 100, 2
Finland	Aventis Pharma Oy Huopalahdentie 24 - 00350 Finland tel. +358 201 200 300/ tel. +358 201 200 354 Liisa Hurme Fax +358 201 200 495 email: liisa.hurme@aventis.com	Nimed	3 %	Gel	Cutaneous use	Tube	30 g, 50 g, 100g, 15 g

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Finland	Aventis Pharma Oy Huopalahdentie 24 - 00350 Finland tel. +358 201 200 300/ tel. +358 201 200 354 Liisa Hurme Fax +358 201 200 495 email: liisa.hurme@aventis.com	Nimed	100 mg	Granules single-dose	Oral use	Sachet	20, 60
France	Laboratoires Therabel Lucien Pharma 123, rue Jules Guesde - 92309 Levallois-Perret Cedex France Tel.+33 1 47 56 69 00 - Fax :+33 1 47 56 69 99	Nexen	100 mg	Tablet	Oral use	Blister	3 X 10
France	Laboratoires Therabel Lucien Pharma 123, rue Jules Guesde - 92309 Levallois-Perret Cedex France Tel.+33 1 47 56 69 00 - Fax :+33 1 47 56 69 99	Nexen	100 mg	Granules	Oral use	Sachet	30
France	Laboratoires Helsinn Healthcare S.A. Via Pian Scairolo - 6912 – Pazzallo -SUISSE Tel. +41 91 985 21 21 - Fax :+41 91 993 21 22 GFU@helsinn.com - RB@helsinn.com	Oxetian	100 mg	Tablet	Oral use	Blister	3 X 10
France	Laboratoires Helsinn Healthcare S.A. Via Pian Scairolo - 6912 – Pazzallo -SUISSE Tel. +41 91 985 21 21 - Fax :+41 91 993 21 22 GFU@helsinn.com - RB@helsinn.com	Oxetian	100 mg	Granules	Oral use	Sachet	30
Greece	Boehringer Ingelheim Hellas Ae 2 Elinixou Street - G-16777 Athens Tel. +30 210 89 06 300 - Fax. +30 210 89 83 207	Mesulid	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Boehringer Ingelheim Hellas Ae 2 Elinixou Street - G-16777 Athens Tel. +30 210 89 06 300 - Fax. +30 210 89 83 207	Mesulid	200 mg	Suppository	Rectal use	Strip	1x6
Greece	Boehringer Ingelheim Hellas Ae 2 Elinixou Street - G-16777 Athens Tel. +30 210 89 06 300 - Fax. +30 210 89 83 207	Mesulid	100 mg	Granules	Oral use	Sachet	1x20
Greece	Boehringer Ingelheim Hellas Ae 2 Elinixou Street - G-16777 Athens Tel. +30 210 89 06 300 - Fax. +30 210 89 83 207	Mesulid	3%	Gel	Cutaneous use	Tube	15g, 30g, 50g, 100g

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Farmedia Ae G. Lira 25 - 14564 Kifisia - Athens Tel. +30 210 62 01 075- Fax. +30 210 62 00 706	Multiformil	100 mg	Tablet	Oral use	Blister	2x10 3x10 5x10
Greece	Pharmaten Epe Basil. Katsos-Derbenakion 6 - Pallini- Greece – GR 15351 Tel.+30 210 666 66 10 -Fax. +30 210 6666749	Bioxidol	100 mg	Granules	Oral use	Sachet	1x30
Greece	Pharmaten Epe Basil. Katsos-Derbenakion 6- Pallini- Greece – GR 15351 Tel.+30 210 666 66 10 - Fax. +30 210 6666749	Bioxidol	100 mg	Tablet	Oral use	Blister	1x20 3x10
Greece	Specifar S.A. T. Basilopoulos -El.Benizelou 11 AG. Barbara – Greece – GR 12351 Tel. +30 210 53 92 700/5692700- Fax. +30 210 56 21 520	Specilid	100 mg	Tablet	Oral use	Blister	3x10 2x10 5x10
Greece	Biospray Abee 45 V. ougo Street - G-10437 Athens Tel. +30 210 52 23 439 - Fax. +30 210 56 21 520	Flogostop	100 mg	Tablet	Oral use	Blister	2x10 3x10 5x10
Greece	Biomedica-Chemica S.A. 25, G. Lira Str. (parodos AG. Fanouriou) 145-64 K. Kifissia, Athens, Greece Tel. +30 210 62 01 075-6/ 6200704-5/ Fax. +30 210 62 00 706	Nimesulide/ Biomedica Chemica	100 mg	Tablet	Oral use	Blister	2x10 3x10 5x10
Greece	Leovan M. Aedn & Cia EE 22, Argonayton Str. Argyroupoli T.K. 164 52 Athens Tel. +30 210 96 04 909 - Fax. +30 210 960 30 95	Ristolzit	100 mg	Tablet	Oral use	Blister	1x20 1x30
Greece	Norma Hellas AE Papazoglou-Menandrou 54 -G-10431 Athens Tel. +30 210 522 6457- Fax. +30 210 52 41 368	Myxina	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Genepharm S.A.18th oxil. Athens Marathonos G-15351 Palini Tel. +30 210 60 39 336 - Fax. +30 210 60 39 402 Dr. Sgoura - d.sgoura@genepharm.gr	Nimelide	100mg	Tablet	Oral use	Blister	2x10 3x10 5x10

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Bros E.P.E. Il.Efthimopoulos- Avgis & Galinis 15 G-15464 N. Kifissia Tel. +30 210 80 72 450-71579/ Fax. +30 210 62 02 211	Discorid	100 mg	Tablet	Oral use	Blister	2x10 5x10
Greece	Rafarm AEBE Nik. Rassias - Kapodistriou and Korintou 12 G-15451 N. Psichixo Athens Tel. +30 210 67 76 550-1/ Fax. +30 210 67 76 552 Ms Irene Rassia: i.rassia@rafarm.gr	Ventor	100 mg	Granules	Oral use	Sachet	1x30
Greece	Rafarm AEBE Nik. Rassias - Kapodistriou and Korintou 12 G-15451 N. Psichixo Athens Tel. +30 210 67 76 550-1/ Fax. +30 210 67 76 552-	Ventor	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Chrispa Alfa Pharma A.E. Andr.Leon-Menandrou 58 - G-Athina Tel. +30 210 52 42221-5223321-6669711 Fax. +30 210 524 89 63	Alencast	100 mg	Tablet	Oral use	Blister	2x10 3x10 5x10
Greece	G.A. Pharmaceuticals S.A. 46 Agisilaou st. - G-173-41 Agios Dimitrios, Athens Tel. +30 210 93 10 980-4/ Fax. +30 210 93 38 759 Sassanis Nikolaos- Hatzi Ageliki gap@ath.forthnet.gr	G-Revm	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Viofar E.P.E. Ethn. Antistaseos and triphilias 76A Acharnai GR 13671 Tel. +30 210 24 68 725/ Fax. +30 210 24 61 937 viofar@otenet.gr	Volonten	100 mg	Tablet	Oral use	Blister	2x10 5x10
Greece	Kleva E.P.E. 189 L. Parnithos Avenue/ G-13671 Acharnai Attiki Tel. +30 210 24 0 2404-7/-246373 Fax. +30 210 2460206 Eleni Polydefkidoy- Manolas Ioannis kleva@hol.gr	Elinap	100 mg	Tablet	Oral use	Blister	3x10 5x10 1x20

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Kleva E.P.E. 189 L. Parnithos Avenue G-13671 Acharnai Attiki Tel. +30 210 24 0 2404-7 Fax. +30 210 2460206	Elinap	100 mg	Powder	Oral use	Sachet	(1x20)x100mg
Greece	Minerva Farmakeytikh A.E. 132Kifissou Avenue - Peristeri - G-121 31 Athens Tel. +30 210 –5702199- Fax. +30 210 57 28 215 www.minervapharm.gr	Min-A-Pon	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Anfarm Hellas A.E. Ap.Nikolaou- K.Palaiologou & Perikleous Xalandri- 442 Acharnon – Athens - G-11143 Tel. +30 210 68 31 632 -21 81 901	Lemesil	100 mg	Tablet	Oral use	Blister	1x20 3x10
Greece	Elpen Pharmaceuticals Co., Inc. 95, Marathonos Ave. G-19009 Pikermi Attikis Tel. +30 210 60 39 326-9/ Fax. +30 210 60 39 300 Kostas Pentafragas- Efie Athanassopoulou elpenmain@hol.gr	Rolaket	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Elpen Pharmaceuticals Co., Inc. 95, Marathonos Ave. G-19009 Pikermi Attikis Tel. +30 210 60 39 326-9/ Fax. +30 210 60 39 300	Rolaket	200 mg	Suppository	Rectal use	Strip	1x6
Greece	Antor Ltd. 4 Omirou Street - G-15126 Marousi Tel. +30 210 61 96 856 - Fax. +30 210 61 96 450	Melimont	100 mg	Tablet	Oral use	Blister	2x10
Greece	Help E.P.E. Evag.Zekkas-Balaoritou 4 - G-14452 Metamorfosi Attikis Tel. +30 210 28 15 353-2843-479 - Fax: +30 210 28 11 850	Mosuolit	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Foiniefarm E.P.E. 5 Anavritis street - G-11143 Athens Tel. +30 210 20 25 813- Fax. +30 210 21 11 528	Kartal	100 mg	Tablet	Oral use	Blister	1x20 1x30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Proel Epam. G. Coronis S.A. 9, Dilou Street - G-12134 Peristeri Tel. +30 210 57 55711-12 / Fax. +30 210 57 48 398 D. Dalls/ G. Coronis registration@proel.gr	Fladalgin	100 mg	Tablet	Oral use	Bottle	1x20 1x30
Greece	Remek A.E. 3 Koleti Str.- 14452 Metamorphosi Attiki - Greece Tel. +30 210 2843581-3/ Fax. +30 210 2843580 - apivita@apivita.gr	Mesupon	100 mg	Tablet	Oral use	Bottle	1x20 1x30
Greece	Remek A.E. 3 Koleti Str.- 14452 Metamorphosi Attiki - Greece Tel. +30 210 2843581-3/ Fax. +30 210 2843580 apivita@apivita.gr	Mesupon	200 mg	Suppository	Rectal use	Strip	1x6
Greece	Iasis Chemipharma AE Agiou Konstantinou - G-15124 Maroussi Tel. +30 210 619 68 95/ Fax: +30 210 61 96 896	Chemisulide	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Remedina A.E. Gounari 23 and Areos - G-13451 Kamatero Attiki Tel. +30 210 23 85 979/552 - Fax. +30 210 23 11 355 Costantinos Theophanopoulos - Irenen Stamopoulou remedina@otenet.gr	Amocetin	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Cosmopharm E.P.E Kazarma Korinthou - P.O. Box 42 - 201 00 Korinthos Greece Tel. +30 2 741 02 53 70/ Fax. +30 2 741 071 685 cosmofarm@hol.gr	Lizepat	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Demo Abee St. Demos - 21 oxil Athinon-Lamias-Krioneri G-14568 Athene Tel. +30 210 81 61 824-802-880/ Fax. +30 210 81 61 587 Yannis Filippakis - yphilippakis@demo.gr	Ritamine	100 mg	Tablet	Oral use	Blister	2x10 3x10

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Medhel Hellas AE 30st klm Athens Laurio- MarkoPoyao - Attikis - Greece 19003 Tel. +30 2299022343- Fax. +30 2299022347 medhel@oneway.gr - Mr. Vassilis Kylicas	Niberan	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Novexal Ellas Ltd Agiou Dimitriou 25 174-55 Kalamaki Tel. +30 210 982 88 76 Fax. +30 210 982 72 11 novexal@otenet.gr	Nimesulide Hexal	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Novexal Ellas Ltd Agiou Dimitriou 25 174-55 Kalamaki Tel. +30 210 982 88 76 Fax. +30 210 982 72 11 novexal@otenet.gr	Nimesulide Hexal	100 mg	Powder	Oral use	Sachet	1x20
Greece	Beaka Hellas Aebe 12 Kapodistriou and Kirintou Street/ N. Psichiko G-15451 Tel.+30 210 67 76 550-1/ Fax. +30 210 67 76 552	Naofid	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Doctum Pharmaceutical S.A. K.T. Giokaris & Co./ Marko Pulu 1oxil km G-19002 Peania Attiki Tel. +30 210 664 36 11/ Fax. +30 210 66 43 614	Erlecit	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Vocate Pharma AE 150 Gounari Street / G-16674 Anoglyphada Tel. +30 210 96 24 436/ Fax: +30 210 96 46 582	Tranzicalm	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Medichrom AE 6o xil Paiana-MarkoPoulos/ Attiki G-19003 - Greece Tel. +30 210 66 24 560/ Fax. +30 210 602 0118 medintl@otenet.gr	Nimesul	100 mg	Tablet	Oral use	Blister	3x10
Greece	Faran Laboratories S.A. Achaias & Trizinias/ G-145 64 Nea Kifissia - Athens Tel. +30 210 80 70 002/ Fax.+30 210 80 71 688	Aflogen	100 mg	Tablet	Oral use	Blister	2x10
Greece	P.N. Gerolymatos Health S.A. 13, Asklipiou str./ 145 68 Kryoneri, Athens,	Edrigyl	100 mg	Tablet	Oral use	Blister	1x20 2x10

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
	Greece Tel. +30 21 816 11 07/ Fax. +30 21 816 17 31 pharmaceuticals@gerolymatos.gr						2x20 4x10
Greece	P.N. Gerolymatos Health S.A. 13, Asklipiou str./ 145 68 Kryoneri, Athens, Greece Tel. +30 21 816 11 07/ Fax. +30 21 816 17 31 pharmaceuticals@gerolymatos.gr	Edrigyl	200 mg	Suppository	Rectal use	Strip	1x6
Greece	P.N. Gerolymatos Health S.A. 13, Asklipiou str./ 145 68 Kryoneri, Athens, Greece Tel. +30 21 816 11 07/ Fax. +30 21 816 17 31 pharmaceuticals@gerolymatos.gr	Edrigyl	100 mg	Granules	Oral use	Sachet	1x20
Greece	S.G.IPHARMA C/O Chrispa Andr. LEON Menandrou 58 – Athens G - 10432 Tel. +30 210 666 9711- Fax. +30 210 6031746	Cliovyl	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Lavipharm Hellas AE Agias Marinas Str. - G-19002 Peania Attikis Tel.+30 210 66 91 396/ 395Fax. +30 210 /6691309 Alavera Irene/ Tsiveriotou Maria/ ealavera@lavipharm.gr	Scaflam	100 mg	Tablet	Oral use	Blister	2x10
Greece	Lavipharm Hellas AE Agias Marinas Str. - G-19002 Peania Attikis Tel.+30 210 66 91 396/ 395Fax. +30 210 /6691309 Alavera Irene/ Tsiveriotou Maria/ ealavera@lavipharm.gr	Scaflam	200 mg	Suppository	Rectal use	Strip	1 x 6
Greece	Lavipharm Hellas AE Agias Marinas Str. - G-19002 Peania Attikis Tel.+30 210 66 91 396/ 395Fax. +30 210 /6691309 Alavera Irene/ Tsiveriotou Maria/ ealavera@lavipharm.gr	Scaflam	100 mg	Granules	Oral use	Sachet	1x20
Greece	Coup. Xr.Kouparousos/ Ag.Barbaras 53 - G-17253 Dafni	Melicat	100 mg	Tablet	Oral use	Blister	2x10 3x10 6x10

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
	Tel. +30 210 97 11 061-9714080/ Fax. +30 210 97 60 837						
Greece	Faran Laboratories S.A. Achaias & Trizinias- G145 64 Nea Kifissia - Athens Tel. +30 210 80 70 002 - Fax.+30 210 80 71 688	Lalide	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Uni-Pharma Abee Ioul.Tseti - 14 o xil.Ethnikis Odou 1/ G-14564 Kifisia Tel. +30 210 80 72 512- Fax. +30 210 80 78 907 Elisabeth Prodromou/ registration@uni-pharma.gr	Dolostop	100 mg	Tablet	Oral use	Bottle	1x20 1x30
Greece	Uni-Pharma Abee Ioul.Tseti - 14 o xil.Ethnikis Odou 1/ G-14564 Kifisia Tel. +30 210 80 72 512- Fax. +30 210 80 78 907 Elisabeth Prodromou/ registration@uni-pharma.gr	Dolostop	100 mg	Granules	Oral use	Sachet	1x20 (2 g)
Greece	Uni-Pharma Abee Ioul.Tseti - 14 o xil.Ethnikis Odou 1/ G-14564 Kifisia Tel. +30 210 80 72 512- Fax. +30 210 80 78 907 Elisabeth Prodromou/ registration@uni-pharma.gr	Dolostop	200 mg	Suppository	Rectal use	Strip	1x6
Greece	Iapharm O.E. - C/O: VILCO Andr Kotsopoulos- PEFKON 121 - Hraklio Attiki G - 14122 Tel. +30 210 284 66 35/ Fax. +30 210 28 13 231	Algover	100 mg	Tablet	Oral use	Blister	2x10 3x10
Greece	Aurora Pharmaceuticals Ltd. 105 Marathonos avenue Gerakas- G-15344 Athens Greece Tel. +30 210 60 49 970/ Fax. +30 210 60 49 971	Auromelid	100 mg	Tablet	Oral use	Blister	3x10
Greece	Pharmanel Pharmaceuticals S. A 106 Marathonos AV, - Gerakas 153 44, Greece Tel: (+30-210-6048560- Fax: +30-210-6613013	Sudinet	100 mg	Tablet	Oral use	Blister	3x10
Greece	Med-One S.A. 211 Parnithos Avenue - G-13671 Acharnai - Attiki Tel. +30 210240 24 05/ Fax. +30 2102 46 02 06	Algosulid	100 mg	Tablet	Oral use	Blister	1x20 1x30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
	Polydefkidoy Eleni						

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Med-One S.A. 211 Parnithos Avenue - G-13671 Acharnai - Attiki Tel. +30 210240 24 05/ Fax. +30 2102 46 02 06 Polydefkidoy Eleni	Algosulid	100 mg	Powder	Oral use	Sachet	1x20
Ireland	Helsinn Birex Pharmaceuticals Damastown, Mulhuddart - Dublin 15/ Ireland Tel. +353 1 822 54 04 - Fax +353 1 822 54 10	Aulin	100 mg	Tablet	Oral use	Blister	15,30,60
Ireland	Helsinn Birex Pharmaceuticals Damastown, Mulhuddart - Dublin 15/ Ireland Tel. +353 1 822 54 04 - Fax +353 1 822 54 10	Aulin	100 mg	Granules	Oral use	Sachet	30
Ireland	Helsinn Birex Pharmaceuticals Damastown, Mulhuddart - Dublin 15/ Ireland Tel. +353 1 822 54 04 - Fax +353 1 822 54 10	Aulin	3 %	Gel	Cutaneous use	Tube	15g, 30 g, 50g, 100 g
Ireland	Helsinn Birex Pharmaceuticals Damastown, Mulhuddart - Dublin 15/ Ireland Tel. +353 1 822 54 04 - Fax +353 1 822 54 10	Mesulid	100 mg	Granules	Oral use	Sachet	1x30
Ireland	Helsinn Birex Pharmaceuticals Damastown, Mulhuddart - Dublin 15/ Ireland Tel. +353 1 822 54 04 - Fax +353 1 822 54 10	Mesulid	100 mg	Tablet	Oral use	Blister	15,30,60
Ireland	Helsinn Birex Pharmaceuticals Damastown, Mulhuddart - Dublin 15/ Ireland Tel. +353 1 822 54 04 - Fax +353 1 822 54 10	Mesulid	3 %	Gel	Cutaneous use	Tube	30 g, 50 g, 100 g
Italy	Roche S.p.A. Via G.B. Stucchi 11020052 Monza (Mi) Italy tel. +39 039 2474620 - fax: +39 039 2474740 Dr. Maurizio Giaracca- Sig. Alessandro Chiariotti Maurizio.giaracca@roche.com	AULIN	100 mg	Tablet	Oral use	Blister	30
Italy	Roche S.p.A. Via G.B. Stucchi 11020052 Monza (Mi) Italy tel. +39 039 2474620 - fax: +39 039 2474740 Dr. Maurizio Giaracca- Sig. Alessandro Chiariotti Maurizio.giaracca@roche.com	AULIN	3%	Gel	Cutaneous use	Tube	30,100 g.

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Roche S.p.A. Via G.B. Stucchi 11020052 Monza (Mi) Italy tel. +39 039 2474620 - fax: +39 039 2474740 Dr. Maurizio Giaracca- Sig. Alessandro Chiariotti Maurizio.giaracca@roche.com	AULIN	50 mg	Granules	Oral use	Sachet	30
Italy	Roche S.p.A. Via G.B. Stucchi 11020052 Monza (Mi) Italy tel. +39 039 2474620 - fax: +39 039 2474740 Dr. Maurizio Giaracca- Sig. Alessandro Chiariotti Maurizio.giaracca@roche.com	AULIN	100 mg	Granules	Oral use	Sachet	30
Italy	Roche S.p.A. Via G.B. Stucchi 11020052 Monza (Mi) Italy tel. +39 039 2474620 - fax: +39 039 2474740 Dr. Maurizio Giaracca- Sig. Alessandro Chiariotti Maurizio.giaracca@roche.com	AULIN	200 mg	Suppository	Rectal use	Strip	10
Italy	Roche S.p.A. Via G.B. Stucchi 11020052 Monza (Mi) Italy tel. +39 039 2474620 - fax: +39 039 2474740 Sig. Alessandro Chiariotti/ Maurizio.giaracca@roche.com	AULIN	3%	Gel	Cutaneous use	Tube	50 g
Italy	Roche S.p.A. Via G.B. Stucchi 11020052 Monza (Mi) Italy tel. +39 039 2474620 - fax: +39 039 2474740 Dr. Maurizio Giaracca- Sig. Alessandro Chiariotti Maurizio.giaracca@roche.com	AULIN BETA	400 mg	Tablet	Oral use	Blister	30
Italy	Roche S.p.A. Via G.B. Stucchi 11020052 Monza (Mi) Italy tel. +39 039 2474620 - fax: +39 039 2474740 Dr. Maurizio Giaracca- Sig. Alessandro Chiariotti Maurizio.giaracca@roche.com	AULIN BETA	400 mg	Granules	Oral use	Sachet	30
Italy	Novartis Farma S.p.A S.S. 233 (Varesina) Km 20,5 - 21040 Origgio (VA) – Italy tel: +39 02 96542214 / fax:+39 02 9659066 Dott.a Lambiase: maria_grazia.vaccari@pharma.novartis.com	MESULID	100 mg	Tablet	Oral use	Blister	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Novartis Farma S.p.A S.S. 233 (Varesina) Km 20,5 - 21040 Origgio (VA) – Italy tel: +39 02 96542214 / fax:+39 02 9659066	MESULID MITE	50 mg	Granules	Oral use	Sachet	30
Italy	Novartis Farma S.p.A S.S. 233 (Varesina) Km 20,5 - 21040 Origgio (VA) – Italy tel: +39 02 96542214 / fax:+39 02 9659066	MESULID	100 mg	Granules	Oral use	Sachet	30
Italy	Novartis Farma S.p.A S.S. 233 (Varesina) Km 20,5 - 21040 Origgio (VA) – Italy tel: +39 02 96542214 / fax:+39 02 9659066	MESULID	200 mg	Suppository	Rectal use	Strip	10
Italy	Novartis Farma S.p.A S.S. 233 (Varesina) Km 20,5 - 21040 Origgio (VA) – Italy tel: +39 02 96542214 / fax:+39 02 9659066	MESULID	3%	Gel	Cutaneous use	Tube	30 g, 50 g 100 g
Italy	Novartis Farma S.p.A S.S. 233 (Varesina) Km 20,5 - 21040 Origgio (VA) – Italy tel: +39 02 96542214 / fax:+39 02 9659066	MESULID FAST	400 mg	Granules	Oral use	Sachet	30; 8;
Italy	Novartis Farma S.p.A S.S. 233 (Varesina) Km 20,5 - 21040 Origgio (VA) – Italy tel: +39 02 96542214 / fax:+39 02 9659066	MESULID FAST	400 mg	Tablet	Oral use	Blister	30
Italy	Italfarmaco S.p.A Via Dei Lavoratori, 54 - 20092 Cinisello Balsamo (MI) – Italy tel. + 39 02 64432500 / fax. + 39 02 64432503	NIMEDEX	400 mg	Granules	Oral use	Sachet	30
Italy	Italfarmaco S.p.A Via Dei Lavoratori, 54 - 20092 Cinisello Balsamo (MI) – Italy tel. + 39 02 64432500 / fax. + 39 02 64432503	NIMEDEX	400 mg	Tablet	Oral use	Blister	30
Italy	SIAR PHARMA Via Verdi 33- 20060 Bussero (Milan) Italy Dr.ssa Sonia Macchelli/ S.ra Marina Pasqualini +39 02 95 33 4270/ +39 02 95 40 91 81 siarpharma@libero.it	ALGOLIDER	100 mg	Tablet	Oral use	Blister	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	SIAR PHARMA Via Verdi 33- 20060 Bussero (Milan) Italy Dr.ssa Sonia Macchelli/ S.ra Marina Pasqualini +39 02 95 33 4270/ +39 02 95 40 91 81 siarpharma@libero.it	ALGOLIDER	100 mg	Granules	Oral use	Sachet	30
Italy	Istituto Chimico Internazionale Dr. Giuseppe Rende S.r.l. Via Salaria, 1240- 00138 Roma –Italy tel: +39 06 8889655 - fax:39 06 8889849	RESULIN	100 mg	Tablet	Oral use	Blister	30
Italy	Istituto Chimico Internazionale Dr. Giuseppe Rende S.r.l. Via Salaria, 1240- 00138 Roma –Italy tel: +39 06 8889655 - fax:39 06 8889849	RESULIN	100 mg	Granules	Oral use	Sachet	30
Italy	Istituto Chimico Internazionale Dr. Giuseppe Rende S.r.l. Via Salaria, 1240- 00138 Roma –Italy tel: +39 06 8889655 - fax:39 06 8889849	RESULIN	200 mg	Suppository	Rectal use	Strip	10
Italy	Laboratori Prodotti Farmaceutici Boniscontro e Gazzone SRL Via Tiburtina, 1004- 00156 Roma – Italy tel. +39 06 4111087 - fax: +39 06 4111603	LEDOREN	100 mg	Tablet	Oral use	Blister	30
Italy	Laboratori Prodotti Farmaceutici Boniscontro e Gazzone SRL Via Tiburtina, 1004- 00156 Roma – Italy tel. +39 06 4111087 - fax: +39 06 4111603	LEDOREN	100 mg	Granules	Oral use	Sachet	30
Italy	Farmaceutici Caber S.p.A. Viale Città d'Europa, 681- 00144 Roma Italy tel. +39 06 52207244 - fax. +39 06 52205488 Dr. Roberto Rosso - info@caber.it	NIMS	100 mg	Tablet	Oral use	Blister	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Farmaceutici Damor S.p.A. Via E. Scaglione, 27 - I-80145 Napoli tel. +39 081 2389001 - fax. +39 081 7405172 Dr Antonella Bassi : dirmed@farmadamor.com	SULIDAMOR	100 mg	Granules	Oral use	Sachet	30
Italy	Farmaceutici Damor S.p.A. Via E. Scaglione, 27 - I-80145 Napoli tel. +39 081 2389001 - fax. +39 081 7405172 Dr Antonella Bassi : dirmed@farmadamor.com	SULIDAMOR	200 mg	Suppository	Rectal use	Strip	10
Italy	NCSN Farmaceutici s.r.l. Via Svetonio 15 - 00136 Roma Tel+Fax. +39 06 35497 652	FANSIDOL	100 mg	Capsule	Oral use	Blister	30
Italy	NCSN Farmaceutici s.r.l. Via Svetonio 15 - 00136 Roma Tel+Fax. +39 06 35497 652	FANSIDOL	100 mg	Granules	Oral use	Sachet	30
Italy	I.BIR.N. – Istituto Bioterapico Nazionale S.r.l. Via V. Grassi, 9/11/13/15 - 00155 Roma – Italy tel. +39 06 2291945 - fax. +39 06 2290849 F. Giannantoni - Ibirn1@infinito.it	NIDE	100 mg	Hard capsule	Oral use	Blister	30
Italy	I.BIR.N. – Istituto Bioterapico Nazionale S.r.l. Via V. Grassi, 9/11/13/15 - 00155 Roma – Italy tel. +39 06 2291945 - fax. +39 06 2290849	NIDE	100 mg	Granules for oral solution	Oral use	Sachet	30
Italy	Laboratorio Farmaceutico C.T. S.r.l. Via Dante Alighieri, 71 - 18038 Sanremo (IM) – Italy tel. +39 0184 59241 - fax. +39 0184 5924216 Dr. Lorenza Guano/ Dr. Roberto Cacciaglia Direz.scientifica@labct.it	FLOLID	100 mg	Tablet	Oral use	Blister	30
Italy	Laboratorio Farmaceutico C.T. S.r.l. Via Dante Alighieri, 71 - 18038 Sanremo (IM) – Italy tel. +39 0184 59241 - fax. +39 0184 5924216	FLOLID	200 mg	Suppository	Rectal use	Strip	10
Italy	Laboratorio Farmaceutico C.T. S.r.l. Via Dante Alighieri, 71 - 18038 Sanremo (IM) – Italy tel. +39 0184 59241 - fax. +39 0184 5924216	FLOLID	100 mg	Granules for oral solution	Oral use	Sachet	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Vecchi & C. Piam S.P.A. Via Padre G. Semeria, 5 - 16131 Genova – Italy tel. +39 010 357234/237/241 - fax. +39 010 355734	REMOV	100 mg	Tablet	Oral use	Blister	30
Italy	Vecchi & C. Piam S.P.A. Via Padre G. Semeria, 5 - 16131 Genova – Italy tel. +39 010 357234/237/241 - fax. +39 010 355734	REMOV	100 mg	Granules	Oral use	Sachet	30
Italy	UCB PHARMA S.p.A. Via Praglia, 15 - 10044 Pianezza (Torino) tel. +39 011 966 01 - fax. +39 011 9660237 Dr. Walter Bianchi- Dr. Laura Chiodini Walter.bianchi@UCB-Group.com	NIMESULIDE UCB	100 mg	Tablet	Oral use	Blister	30
Italy	UCB PHARMA S.p.A. Via Praglia, 15 - 10044 Pianezza (Torino) tel. +39 011 966 01 - fax. +39 011 9660237 Dr. Walter Bianchi- Dr. Laura Chiodini Walter.bianchi@UCB-Group.com	NIMESULIDE UCB	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Essetti Farmaceutici S.p.A. Via Cavalli di Bronzo, 41 - S. Giorgio a Cremano (Napoli) I-80046 – Italy tel. +39 081 5658111 - fax. +39 081 482834	LAIDOR	50 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Essetti Farmaceutici S.p.A. Via Cavalli di Bronzo, 41 - S. Giorgio a Cremano (Napoli) I-80046 – Italy tel. +39 081 5658111 - fax. +39 081 482834	LAIDOR	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Essetti Farmaceutici S.p.A. Via Cavalli di Bronzo, 41 - S. Giorgio a Cremano (Napoli) I-80046 – Italy tel. +39 081 5658111 - fax. +39 081 482834	LAIDOR	100 mg	Tablet	Oral use	Blister	30
Italy	Laboratori Guidotti S.p.A. Via Trieste, 40 - 56126 Pisa – Italy tel. + 39 050 505211 - fax. +39 050 49340	NIMESULENE	100 mg	Tablet	Oral use	Blister	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Laboratori Guidotti S.p.A. Via Trieste, 40 - 56126 Pisa – Italy tel. + 39 050 505211 - fax. +39 050 49340	NIMESULENE	100 mg	Powder for oral solution	Oral use	Sachet	30
Italy	Laboratori Guidotti S.p.A. Via Trieste, 40 - 56126 Pisa – Italy tel. + 39 050 505211 - fax. +39 050 49340	NIMESULENE	200 mg	Suppository	Rectal use	Strip	10
Italy	Francia Farmaceutici Industria Farmaco Biologica S.r.l. Via dei Pestagalli, 7/ 20138 Milano – Italy tel. +39 02 502290 / fax. +39 02 58012252 Nastro.FranciaFarm@iol.it - Cassis.FranciaFarm@iol.it	ALGIMESIL	100 mg	Granules for oral solution	Oral use	Sachet	30
Italy	Francia Farmaceutici Industria Farmaco Biologica S.r.l. Via dei Pestagalli, 7/ 20138 Milano – Italy tel. +39 02 502290 / fax. +39 02 58012252 Nastro.FranciaFarm@iol.it - Cassis.FranciaFarm@iol.it	ALGIMESIL	100 mg	Tablet	Oral use	Blister	30
Italy	Infosint S.p.A. Via della Filanda, 5 20060 Gessate (Milano) Tel. +39 02 959 211 Fax: +39 02 959 219 e-mail: infosint@tiscalinet.it Dr. Vincenzo Olgiati	SULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Infosint S.p.A. Via della Filanda, 5 20060 Gessate (Milano) Tel. +39 02 959 211 Fax: +39 02 959 219 e-mail: infosint@tiscalinet.it Dr. Vincenzo Olgiati	SULIDE	100 mg	Granules	Oral use	Sachet	30
Italy	Infosint S.p.A. Via della Filanda, 5 20060 Gessate (Milano) Tel. +39 02 959 211 Fax: +39 02 959 219 e-mail: infosint@tiscalinet.it Dr. Vincenzo Olgiati	SULIDE	200 mg	Suppository	Rectal use	Strip	10

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	ERREKAPPA Euroterapici S.p.A. Via Ciro Menotti 1/A - 20129 Milano – Italy tel. +39 02 7491345 -fax. +39 02 715734	SULMEDIL	100 mg	Tablet	Oral use	Blister	30
Italy	ERREKAPPA Euroterapici S.p.A. Via Ciro Menotti 1/A - 20129 Milano – Italy tel. +39 02 7491345 -fax. +39 02 715734	SULMEDIL	100 mg	Granules	Oral use	Sachet	30
Italy	ERREKAPPA Euroterapici S.p.A. Via Ciro Menotti 1/A - 20129 Milano – Italy tel. +39 02 7491345 -fax. +39 02 715734	SULMEDIL	200 mg	Suppository	Rectal use	Strip	10
Italy	Mipharm S.p.A. Via Bernardo Quaranta, 12 - 20141 Milano – Italy tel. +39 02 535481 - fax. +39 02 53548010 www.mipharm.it - Dr. Giorgio Corsico	TEONIM	100 mg	Granules	Oral use	Sachet	30
Italy	Mipharm S.p.A. Via Bernardo Quaranta, 12 - 20141 Milano – Italy tel. +39 02 535481 - fax. +39 02 53548010 www.mipharm.it - Dr. Giorgio Corsico	TEONIM	100 mg	Tablet	Oral use	Blister	30
Italy	Istituto Luso Farmaco d'Italia S.p.A. Via Walter Tobagi, 8 20068 Peschiera Borromeo (Milano) Tel. +39 02 516 55 51 Fax: +39 02 516 50 550	NIMESIL	100 mg	Granules	Oral use	Sachet	30
Italy	Istituto Biochimico Nazionale Savio S.r.l. Viale Città d'Europa, 681 - 00144 Roma Italy tel. +39 06 –52207244 - fax. +39 06 52205488 Dr. Roberto Rosso - info@caber.it	EUDOLENE	100 mg	Granules	Oral use	Sachet	30
Italy	Levofarma S.r.l. Via Conforti, 42 - 84083 Castel San Giorgio (SA) – Italy Tel. +39 081 5162315 - fax. +39 081 5161590 Angelo Mele - mail@farma.uno.it	NOALGOS	100 mg	Granules	Oral use	Sachet	30
Italy	Levofarma S.r.l. Via Conforti, 42 - 84083 Castel San Giorgio (SA) – Italy Tel. +39 081 5162315 - fax. +39 081 5161590	NOALGOS	100 mg	Tablet	Oral use	Blister	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	So.Se. Pharm S.r.l. Via dei Castelli Romani, 22- 00040 Pomezia (Roma) – Italy tel. +39 06 91140153 - fax. +39 06 91603462	DOMES	100 mg	Granules	Oral use	Sachet	30
Italy	So.Se. Pharm S.r.l. Via dei Castelli Romani, 22- 00040 Pomezia (Roma) – Italy tel. +39 06 91140153 - fax. +39 06 91603462	DOMES	100 mg	Tablet soluble	Oral use	Blister	30
Italy	So.Se. Pharm S.r.l. Via dei Castelli Romani, 22- 00040 Pomezia (Roma) – Italy tel. +39 06 91140153 - fax. +39 06 91603462	DOMES	100 mg	Tablet	Oral use	Blister	30
Italy	Selvi Laboratorio Bioterapico S.p.A. Via Proio 28 Fiano Romano 00065 Roma Tel: 39 076 545 5718- Fax: 39 0765 455 633	ANTALGO	100 mg	Tablet	Oral use	Blister	30
Italy	Selvi Laboratorio Bioterapico S.p.A. Via Proio 28 Fiano Romano 00065 Roma Tel: 39 076 545 5718- Fax: 39 0765 455 633	ANTALGO	100 mg	Granules for oral solution	Oral use	Sachet	30
Italy	GNR S.p.A. S.S. 233 Varesina - Km 20,5 - 21040 Origgio (Va) Italy tel +39 02 9654 3483 - Fax. +39 02 9654 3495	NIMESULIDE	100 mg	Granules for oral solution	Oral use	Sachet	30
Italy	GNR S.p.A. S.S. 233 Varesina - Km 20,5 - 21040 Origgio (Va) Italy tel +39 02 9654 3483 - Fax. +39 02 9654 3495	NIMESULIDE	100 mg	Hard capsule	Oral use	Blister	30
Italy	Dompè Farmaceutici S.p.A. Via San Martino 12 – 12/A - 20122 Milano – Italy tel. +39 02 58383256 - fax. +39 02 58383324 enrico.bosone@dompe.it - Roberta Villa	NISAL	100 mg	Granules	Oral use	Sachet	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Dompè Farmaceutici S.p.A. Via San Martino 12 – 12/A - 20122 Milano – Italy tel. +39 02 58383256 - fax. +39 02 58383324 enrico.bosone@dompe.it - Roberta Villa	NISAL	100 mg	Capsule	Oral use	Blister	30
Italy	Pulitzer Italiana S.r.l.Via Tiburtina 1004 00156 Roma – Italy tel +39 06 4111087 - fax +39 06 4111603	LEDOLID	100 mg	Tablet	Oral use	Blister	30
Italy	Pulitzer Italiana S.r.l.Via Tiburtina 1004 00156 Roma – Italy tel +39 06 4111087 - fax +39 06 4111603	LEDOLID	100 mg	Granules	Oral use	Sachet	30
Italy	Magis Farmaceutici S.p.A. Via Cacciamali 34-36-38/A - 25125 Brescia – Italy tel. +39 030 349761 - fax. +39 030-349352	ISODOL	100 mg	Granule for oral suspension	Oral use	Sachet	30
Italy	Magis Farmaceutici S.p.A. Via Cacciamali 34-36-38/A - 25125 Brescia – Italy tel. +39 030 349761 - fax. +39 030-349352	ISODOL	100 mg	Tablet	Oral use	Blister	30
Italy	Lampugnani Farmaceutici S.p.A. Via Gramsci, 4 - 20014 Nerviano (MI) – Italy tel. +39 0331 587354 - fax. +39 0331 585588 Doot. Bertacco: info@lampugnanifarmaceutici.it	NOXALIDE	5%	Oral suspension	Oral use	Bottle	60 ml
Italy	Lampugnani Farmaceutici S.p.A. Via Gramsci, 4 - 20014 Nerviano (MI) – Italy tel. +39 0331 587354 - fax. +39 0331 585588	NOXALIDE	100 mg	Granules	Oral use	Sachet	30
Italy	Kruger Pharma S.r.l. Via Volturno, 10-12 50019 Sesto Fiorentino (FI) – Italy tel. +39 055 3024503 - fax. +39 055 3025015	NIMENOL	100 mg	Granules for oral suspension	Oral use	Sachet	15 30
Italy	A.C.R.A.F. S.p.A. Aziende Chimiche Riunite Angelini Francesco- Piazzale della Stazione, snc 00040 S. Palomba Pomezia (Roma) –Italy tel +39 06 91045244 - fax. +39 06 91045299	NIMEXAN	100 mg	Granules	Oral use	Sachet	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	A.C.R.A.F. S.p.A. Aziende Chimiche Riunite Angelini Francesco- Piazzale della Stazione, snc 00040 S. Palomba Pomezia (Roma) –Italy tel +39 06 91045244 - fax. +39 06 91045299	NIMEXAN	200 mg	Suppository	Rectal use	Strip	10
Italy	MDM SpA Via Volturno 29/B - 20052 Monza (MI) – Italy tel. +39 039 322270 - fax. +39 039 322168 mdm@mdmspa.com - M. Trognoni	SOLVING	100 mg	Tablet	Oral use	Blister	30
Italy	MDM SpA Via Volturno 29/B - 20052 Monza (MI) – Italy tel. +39 039 322270 - fax. +39 039 322168	SOLVING	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Aesculapius Farmaceutici S.r.l. Via Cozzaglio, 24 - 25125 Brescia – Italy tel. +39 030 3532013 - fax. +39 030 349352	EFRIDOL	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Aesculapius Farmaceutici S.r.l. Via Cozzaglio, 24 - 25125 Brescia – Italy tel. +39 030 3532013 - fax. +39 030 349352	EFRIDOL	100 mg	Tablet	Oral use	Blister	30
Italy	LA.FA.RE. Laboratorio Farmaceutico Reggiano S.r.l. Via Benedetto. Cozzolino, 77- Ercolano Resina (NA) I-80056 – Italy Tel. +39 081 7390596 - fax. +39 081 7321462	DIMESUL	100 mg	Tablet	Oral use	Blister	30
Italy	LA.FA.RE. Laboratorio Farmaceutico Reggiano S.r.l. Via Benedetto. Cozzolino, 77- Ercolano Resina (NA) I-80056 – Italy Tel. +39 081 7390596 - fax. +39 081 7321462	DIMESUL	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Dorom S.r.l. Via Volturno, 48 20089 Quinto de Stampi Rozzano (MI) – Italy tel. +39 06-59290330 - fax. +39 06 5913128 Dr Fuchs	NIMESULIDE	100 mg	Powder for oral solution	Oral use	Sachet	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Dorom S.r.l. Via Volturno, 48 20089 Quinto de Stampi Rozzano (MI) – Italy tel. +39 06-59290330 - fax. +39 06 5913128 Dr Fuchs	NIMESULIDE	200 mg	Suppository	Rectal use	Strip	10
Italy	Teva Pharma Italia S.r.l. V.le Richard, 7 - 20143 Milano – Italy tel. +39 02 8917981 - fax. + 39 02 89179825	NIMESULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Teva Pharma Italia S.r.l. V.le Richard, 7 - 20143 Milano – Italy tel. +39 02 8917981 - fax. + 39 02 89179825	NIMESULIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Teva Pharma Italia S.r.l. V.le Richard, 7 - 20143 Milano – Italy tel. +39 02 8917981 - fax. + 39 02 89179825	NIMESULIDE	200 mg	Suppository	Rectal use	Strip	10
Italy	Merck-Generics Italia S.p.A. Via Aquileia, 35 - Cisinello Balsamo-(Mi) I-20092-Italy tel + 39 02 6124691 - fax. +39 02 61294448 Dr. Maurizio Schiassi - Dr. Stefania Pulimeno spulimeno@merckgenericsitalia.com	NIMESULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Merck-Generics Italia S.p.A. Via Aquileia, 35 - Cisinello Balsamo-(Mi) I-20092-Italy tel + 39 02 6124691 - fax. +39 02 61294448	NIMESULIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Merck-Generics Italia S.p.A. Via Aquileia, 35 - Cisinello Balsamo-(Mi) I-20092-Italy tel + 39 02 6124691 - fax. +39 02 61294448	NIMESULIDE	200 mg	Suppository	Rectal use	Strip	10
Italy	Merck-Generics Italia S.p.A. Via Aquileia, 35 - Cisinello Balsamo-(Mi) I-20092-Italy tel + 39 02 6124691 - fax. +39 02 61294448	Nimesulide	100 mg	Suppository	Rectal use	Strip	10
Italy	New Research S.r.l P/zza Don Luigi Sturzo 34- 04011 Aprilia (LT) – Italy tel. +39 06 92727688 - fax. +39 06 92727688	NERELID	100 mg	Capsule	Oral use	Blister	

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	New Research S.r.l P/zza Don Luigi Sturzo 34- 04011 Aprilia (LT) – Italy tel. +39 06 92727688 - fax. +39 06 92727688	NERELID	100 mg	Granules for oral solution	Oral use	Sachet	30
Italy	I.B.N. – Istituto Biologico Nazionale S.r.l. Viale Città d'Europa, 681- 00144 Roma Italy tel. +39-6-52205466 - fax. +39-6-52205488 development@ibnsavio.it	NIMESULIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Sintactica S.r.l Viale Ercole Marelli, 352 - 20099 Sesto San Giovanni (MI) It tel. +39 02 95344147 - fax. +39 02 95343990 Dr. Massimiliano Borsa - info@sintactica.it	DOLXTREN	5%	Oral suspension	Oral use	Bottle	60 ml
Italy	Robin S.r.l. Piazzale Durante Francesco, 11 - 20131 Milano – Italy tel. +39 039 2474435 - fax. +39 039 2474630	NIMESULIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Robin S.r.l. Piazzale Durante Francesco, 11 - 20131 Milano – Italy tel. +39 039 2474435 - fax. +39 039 2474630	NIMESULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Farmaceutici Ecobi S.A.S. Via E. Bazzano, 26 - Ronco Scrivia (GE)- I-16019 – Italy tel. +39 010 9651010 - fax. +39 010 9350679	AREUMA	100 mg	Tablet	Oral use	Blister	30
Italy	Farmaceutici Ecobi S.A.S. Via E. Bazzano, 26 - Ronco Scrivia (GE)- I-16019 – Italy tel. +39 010 9651010 - fax. +39 010 9350679	AREUMA	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Farmaceutici Ecobi S.A.S. Via E. Bazzano, 26 - Ronco Scrivia (GE)- I-16019 – Italy tel. +39 010 9651010 - fax. +39 010 9350679	AREUMA	200 mg	Suppository	Rectal use	Strip	10
Italy	DOC Generici S.r.l. Via Manuzio, 7 - 20124 Milano – Italy tel. +39 02 655341 - fax. +39 02 6590611 Franco Cotti - Tiziana Alessi	NIMESULIDE	100 mg	Tablet	Oral use	Blister	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	DOC Generici S.r.l. Via Manuzio, 7 - 20124 Milano – Italy tel. +39 02 655341 - fax. +39 02 6590611 Franco Cotti - Tiziana Alessi Tiziana.alessi@genericidoc.it	NIMESULIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	DOC Generici S.r.l. Via Manuzio, 7 - 20124 Milano – Italy tel. +39 02 655341 - fax. +39 02 6590611 Franco Cotti - Tiziana Alessi Tiziana.alessi@genericidoc.it	NIMESULIDE`	200 mg	Suppository	Rectal use	Strip	10
Italy	EG S.p.A. Via Rondoni, 1 - 20146 Milano – Italy Tel. +39 02 8310371 - Fax : +39 02 831 03776 emagni@eglab@tiscalinet.it	NIMESULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	EG S.p.A. Via Rondoni, 1 - 20146 Milano – Italy Tel. +39 02 8310371 - Fax : +39 02 831 03776 emagni@eglab@tiscalinet.it	NIMESULIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	EG S.p.A. Via Rondoni, 1 - 20146 Milano – Italy Tel. +39 02 8310371 - Fax : +39 02 831 03776 emagni@eglab@tiscalinet.it	NIMESULIDE	100 mg	Effervescent tablet	Oral use	Blister	30
Italy	Ratiopharm GmbH Via Accademia, 26 - 20131 Milano tel. +39 02 288771 - fax. +39 02 28 877 22 Ms Lorena Verza	NIMESULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Ratiopharm GmbH Via Accademia, 26 - 20131 Milano tel. +39 02 288771 - fax. +39 02 28 877 22	NIMESULIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Ratiopharm GmbH Via Accademia, 26 - 20131 Milano tel. +39 02 288771 - fax. +39 02 28 877 22	NIMESULIDE	100 mg	Effervescent tablet	Oral use	Blister	30
Italy	F.D. Farmaceutici S.r.l. Via Donatori del sangue 22 - 26020 Corte de' Cortesi con Cignone (CR) Italy Tel. +39 0372 925050 - Fax +39 0372 925080 Fd.mara@tin.it	DOLESIDE	100 mg	Tablet	Oral use	Blister	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	F.D. Farmaceutici S.r.l. Via Donatori del sangue 22 - 26020 Corte de' Cortesi con Cignone (CR) Italy Tel. +39 0372 925050 - Fax +39 0372 925080 Fd.mara@tin.it	DOLESIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	S.I.F.I. – Società Farmaceutica Italiana S.p.A. Via Ercole Patti, 36 65020 Lavinaio – Aci S.Antonio (CT) – Italy tel. +39 095 7922111 - fax. +39-095-7922250	EDEMAX	100 mg	Tablet	Oral use	Blister	30
Italy	S.I.F.I. – Società Farmaceutica Italiana S.p.A. Via Ercole Patti, 36 65020 Lavinaio – Aci S.Antonio (CT) – Italy tel. +39 095 7922111 - fax. +39-095-7922250	EDEMAX	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Pliva Pharma S.pA. Via dei Giardini, 7 - 20100 Milano – Italy tel. +39 02 66043234 - fax +39 02 61293592	NIMESULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Pliva Pharma S.pA. Via dei Giardini, 7 - 20100 Milano – Italy tel. +39 02 66043234 - fax +39 02 61293592	NIMESULIDE	100 mg	Granules	Oral use	Sachet	30
Italy	Pliva Pharma S.pA. Via dei Giardini, 7 - 20100 Milano – Italy tel. +39 02 66043234 - fax +39 02 61293592	MIGRALESS	100 mg	Tablet for oral suspension	Oral use	Blister	30
Italy	Sofar S.p.A. Via Firenze, 40 - 20060 Trezzano Rosa (MI) – Italy tel. +39 02 90937212 - fax. +39 02 9096 7239	FANSULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Sofar S.p.A. Via Firenze, 40 - 20060 Trezzano Rosa (MI) – Italy tel. +39 02 90937212 - fax. +39 02 9096 7239	FANSULIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Alterna Farmaceutici S.r.l. Via dei Pestagalli Pietro e Giuseppe, 7 20138 Milano – Italy Tel. -Fax.	IDEALID	100 mg	Tablet	Oral use	Blister	30
Italy	Alterna Farmaceutici S.r.l. Via dei Pestagalli Pietro e Giuseppe, 7 20138 Milano – Italy	IDEALID	100 mg	Granules for oral suspension	Oral use	Sachet	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Hexan S.p.A. Piazzale della Stazione - 00040 Santa Palomba (Roma) –Italy tel +39 06 91045244 - fax. +39 06 91045299	NIMESULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Hexan S.p.A. Piazzale della Stazione - 00040 Santa Palomba (Roma) –Italy tel +39 06 91045244 - fax. +39 06 91045299	NIMESULIDE	100 mg	Granules for oral solution	Oral use	Sachet	30
Italy	A.G.I.P.S. Farmaceutici S.p.A. Via Amendola, 4 - 16035 Rapallo (GE) – Italy tel. + 39 0185 58223/4 - fax. + 39 0185 60374	DELFOS	100 mg	Tablet	Oral use	Blister	30
Italy	A.G.I.P.S. Farmaceutici S.p.A. Via Amendola, 4 - 16035 Rapallo (GE) – Italy tel. + 39 0185 58223/4 - fax. + 39 0185 60374	DELFOS	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	P.R.C. S.r.l. Via Conforti, 42 - 84083 Castel San Giorgio (SA) – Italy Tel. +39 081 5162315 - Fax.+39 081 5161590 mail@farmauno.it	LIDERSOLV	100 mg	Tablet	Oral use	Blister	30
Italy	P.R.C. S.r.l. Via Conforti, 42 - 84083 Castel San Giorgio (SA) – Italy Tel. +39 081 5162315 - Fax.+39 081 5161590 mail@farmauno.it	LIDERSOLV	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Nobel Farmaceutici S.r.l. Via Tiburtina, 1004 - I-00156 Roma - Italy Tel +39 06 4111087- Fax. +39 06 4111603	LIDENIX	100 mg	Tablet	Oral use	Blister	30
Italy	Nobel Farmaceutici S.r.l. Via Tiburtina, 1004 - I-00156 Roma - Italy Tel +39 06 4111087- Fax. +39 06 4111603	LIDENIX	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Janssen Cilag SpA Via M. Buonarroti 23 - 20293 Cologno Monzese (Mi) Italy Tel. +39 02 25101 - Fax. +39 02 2670 8196	BEIOND	100 mg	Tablet	Oral use	Blister	30
Italy	Janssen Cilag SpA Via M. Buonarroti 23 - 20293 Cologno Mse (Mi) I Tel. +39 02 25101 - Fax. +39 02 2670 8196	BEIOND	100 mg	Granules	Oral use	Sachet	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Farmaceutici Formenti SpA Via Correggio 43 - 20149 Milano Italy Tel. +39 02 43051 - Fax. +39 02 430555 Email: dg@formenti.it	NIMESULIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Farmaceutici Formenti SpA Via Correggio 43 - 20149 Milano Italy Tel. +39 02 43051 - Fax. +39 02 430555 Email: dg@formenti.it	NIMESULIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	L. Molteni & C. dei F.lli Allitti SpA SS 67- Fraz. Granatieri - 50018 Scandicci (Fi) Italy Tel. +39 055 7361278 Fax. +39 0557 20057/ +39 055 7361272 p.baccetti@moltenifarma.it	Nidemol	100 mg	Sachet	Oral use	Sachet	30
Italy	L. Molteni & C. dei F.lli Allitti SpA SS 67- Fraz. Granatieri - 50018 Scandicci (Fi) Italy Tel. +39 055 7361278 Fax. +39 0557 20057/ +39 055 7361272 p.baccetti@moltenifarma.it	Nidemol	200 mg	Suppository	Rectal use	Strip	10
Italy	Polifarma SpA Via Tor Sapienza 138 - Roma 00155 Italy Tel. +39 06 227420 - Fax. +39 06 227 422 61	Nimesulide	100 mg	Tablet	Oral use	Blister	30
Italy	Polifarma SpA Via Tor Sapienza 138 - Roma 00155 Italy Tel. +39 06 227420 - Fax. +39 06 227 422 61	Nimesulide	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	GET S.r.l.Via Dante Alighieri 73 18038 Sanremo (IM) Italy Tel. +39 0184 59 241 - Fax. +39 0184 5924216 Dr. Lorenza Guano - Dr. Roberto Cacciaglia Direz.scientifica@labct.it	Nimesulide	100 mg	Tablet	Oral use	Blister	30
Italy	GET S.r.l.Via Dante Alighieri 73 18038 Sanremo (IM) Italy Tel. +39 0184 59 241 - Fax. +39 0184 5924216 Dr. Lorenza Guano - Dr. Roberto Cacciaglia Direz.scientifica@labct.it	Nimesulide	100 mg	Granules for oral suspension	Oral use	Sachet	30

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Italy	Prodotti Formenti SRL Via Coreggio 43 - 20149 Milano Italy Tel. +39 02 43051- Fax. +39 02 430555	FLAMINIDE	100 mg	Tablet	Oral use	Blister	30
Italy	Prodotti Formenti SRL Via Coreggio 43 - 20149 Milano Italy Tel. +39 02 43051- Fax. +39 02 430555	FLAMINIDE	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Novartis Consumer Health SpA Largo U. Boccioni 1 - 21040 Origgio (VA) Italy Tel. +39 02 96 47 9586 - Fax. +39 02 96479656 Dr. Maria Carla Baggio - Dr. Carlo Candiani Maria_carla.baggio@ch.novartis.com	Reumalide	100 mg	Granules for oral suspension	Oral use	Sachet	30
Italy	Novartis Consumer Health SpA Largo U. Boccioni 1 - 21040 Origgio (VA) Italy Tel. +39 02 96 47 9586 - Fax. +39 02 96479656 Dr. Maria Carla Baggio - Dr. Carlo Candiani Maria_carla.baggio@ch.novartis.com	Reumalide	200 mg	Suppository	Rectal use	Strip	10
Luxembourg	Therabel Pharma s.a. 108 rue E. Van Ophem - B-1180 Bruxelles Tel. +32 2 370 46 38 - Fax. +32 2 370 46 88	Mesulid	100 mg	Tablet	Oral use	blister	14,30,60 tablets in blister and 30,60 in unit dose
Luxembourg	Therabel Pharma s.a. 108 rue E. Van Ophem - B-1180 Bruxelles Tel. +32 2 370 46 38 - Fax. +32 2 370 46 88	Mesulid	100 mg	Granules	Oral use	sachet	14,30,60
Luxembourg	Therabel Pharma s.a. 108 rue E. Van Ophem - B-1180 Bruxelles Tel. +32 2 370 46 38 - Fax. +32 2 370 46 88	Mesulid	3%	Gel	Cutaneous use	Tube	30g, 50g, 100g
Portugal	Jaba Farmacêutica, S.A. Apartado 165 - Zona Industrial da Abrunheira PT- 2711 901 Sintra T: 00351214329648 F:00351219151930 Maria Joao Marruz - Julio Carvalhal Maria.marruz@jaba.pt Head office: rua da Tapada Grande 2 – Zona Industrial da Abrunheira PT2710-089 Sintra	Nimesulida Jaba 100 mg granulado para solução oral	100 mg	Granules for oral solution	Oral use	Sachet	10; 30 and 60

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Portugal	Angelini Farmacêutica, Lda. - Rua João Chagas n. 53 3° Piso 1495-072 Algés- Portugal T: 00351214148300 F: 00351214142981	Aulin	100 mg	Tablet	Oral use	Blister	14; 30 and 60
Portugal	Angelini Farmacêutica, Lda. - Rua João Chagas n. 53 3° Piso 1495-072 Algés- Portugal T: 00351214148300 F: 00351214142981	Aulin	200 mg	Suppository	Rectal use	Strip	10 and 12
Portugal	Angelini Farmacêutica, Lda. - Rua João Chagas n. 53 3° Piso 1495-072 Algés- Portugal T: 00351214148300 F: 00351214142981	Aulin	100mg	Granules for oral solution	Oral use	Sachet	14; 30 and 60
Portugal	Angelini Farmacêutica, Lda. - Rua João Chagas n. 53 3° Piso 1495-072 Algés- Portugal T: 00351214148300 F: 00351214142981	Aulin Gel	30 mg/g	Gel	Cutaneous use	Tube	30; 50 and 100g
Portugal	Wyeth Lederle Portugal (Farma), Lda. PRTRua Dr. António Loureiro Borges, 2 - Arquiparque Miraflores Algés 1495-131 T: 00351214128200 F: 00351214120111	Donulide	100 mg	Tablet	Oral use	Blister	14; 20; 30 and 60
Portugal	Wyeth Lederle Portugal (Farma), Lda. PRTRua Dr. António Loureiro Borges, 2 - Arquiparque Miraflores Algés 1495-131 T: 00351214128200 F: 00351214120111	Donulide	100 mg	Granules for oral solution	Oral use	Sachet	14; 20; 30 and 60

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Portugal	Wyeth Lederle Portugal (Farma), Lda. PRTRua Dr. A L Borges, 2 - Arquiparque Miraflores Algés 1495-131 T: 00351214128200 F: 00351214120111	Donulide Gel	30 mg/g	Gel	Cutaneous use	Tube	30; 50 and 100g
Portugal	Farmoz - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros, Edif. Sagres, 3° A 2685- 338 Prior Velho T: 00351210414100 - Fax. 00351219410839 Ana Real - Augusto Filipe tecnimedicina@mail.telepac.pt	Flamisul	100 mg	Tablet	Oral use	Blister	10; 30 and 60
Portugal	Farmoz - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros, Edif. Sagres, 3° A 2685- 338 Prior Velho T: 00351210414100 - Fax. 00351219410839 Ana Real - Augusto Filipe tecnimedicina@mail.telepac.pt	Flamisul	100 mg	Granules	Oral use	Sachet	10; 20; 30 and 60
Portugal	Companhia Portuguesa de Higiene, S.A. Rua dos Bem Lembrados, 141 – Manique 2645 – 471 Alcabideche Portugal T:0035121444 96 00 F: 0035121444 96 99/ pharmacovigilance 444 96 40 Francisco Freire-de-andrade, MD - Isabel Machado, Ph fandrade@cph.pt	Gerilide	100 mg	Tablet	Oral use	Blister	10; 20; 30 and 60
Portugal	Companhia Portuguesa de Higiene, S.A. Rua dos Bem Lembrados, 141 – Manique 2645 – 471 Alcabideche Portugal T:0035121444 96 00 F: 0035121444 96 99/ pharmacovigilance 444 96 40 Francisco Freire-de-andrade, MD - Isabel Machado, Ph fandrade@cph.pt	Gerilide	200 mg	Suppository	Rectal use	Strip	10

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Portugal	Companhia Portuguesa de Higiene, S.A. Rua dos Bem Lembrados, 141 – Manique 2645 – 471 Alcabideche Portugal T:0035121444 96 00 F: 0035121444 96 99/ pharmacovigilance 444 96 40 Francisco Freire-de-andrade, MD - Isabel Machado, Ph fandrade@cph.pt	Gerilide	100mg	Granules	Oral use	Sachet	10; 20 and 30
Portugal	Tecnimede - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros - Edf. Sagres, 3º A Prior Velho 2685 338 T: 00351210414100 - F: 00351219410839Ana Real - Augusto Filipe tecnimedicina@mail.telepac.pt	Isartrox	100mg	Tablet	Oral use	Blister	10; 12; 20; 30 and 60
Portugal	Tecnimede - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros - Edf. Sagres, 3º A Prior Velho 2685 338 T: 00351210414100 - F: 00351219410839Ana Real - Augusto Filipe tecnimedicina@mail.telepac.pt	Isartrox	100mg	Granules	Oral use	Sachet	10; 12; 20; 30 and 60
Portugal	Jaba Farmacêutica, S.A. Apartado 165 - Zona Industrial da Abrunheira PT- 2711 Sintra T: 00351214329648 F:00351219151930 Head office: rua da tapada grande, 2 Zona Industrial da Abrunheira 2710 089 Sintra Maria Joao Marruz -Julio Carvalhal Maria-marruz@jaba.pt	Jabasulide	100mg	Tablet	Oral use	Blister	10; , 30 and 60
Portugal	Jaba Farmacêutica, S.A. Apartado 165 - Zona Industrial da Abrunheira PT- 2711 Sintra T: 00351214329648 F:00351219151930 Head office: rua da tapada grande, 2 Zona Industrial da Abrunheira 2710 089 Sintra Maria Joao Marruz- Julio Carvalhal Maria-marruz@jaba.pt	Jabasulide	100mg	Granules for oral solution	Oral use	Sachet	10; 30 and 60

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Portugal	Tecnimede - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros - Edf. Sagres, 3º A Prior Velho 2685 338 T: 00351210414100 - F: 00351219410839Ana Real - Augusto Filipe tecnimedicina@mail.telepac.pt	Neuride	100mg	Tablet	Oral use	Blister	10; 30 and 60
Portugal	Tecnimede - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros - Edf. Sagres, 3º A Prior Velho 2685 338 T: 00351210414100 - F: 00351219410839Ana Real - Augusto Filipe tecnimedicina@mail.telepac.pt	Neuride	100mg	Granules	Oral use	Sachet	10; 20; 30 and 60
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros T: 00351232831100 F: 00351232831112 Alda Rodrigues - labesfal@mail.telepac.pt	Nimalge	100mg	Granules for oral suspension	Oral use	Sachet	10; 20; 30 and 60
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros T: 00351232831100 F: 00351232831112 Alda Rodrigues - labesfal@mail.telepac.pt	Nimalge	200mg	Suppository	Rectal use	Strip	10
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros T: 00351232831100 F: 00351232831112 Alda Rodrigues - labesfal@mail.telepac.pt	Nimalge	100mg	Tablet	Oral use	Blister	10; 20; 30 and 60
Portugal	Mediquímica - Produtos Químicos, Especialidades Farmacêuticas, Lda. Vala do Carregado 2600-726 Castanheira do Ribatejo T: 0351263856800 F: 0351263855020	Nimartin	100mg	Coated Tablet	Oral use	Blister	10; 20; 30 and 60
Portugal	Aventis Pharma, Lda. Estrada Nacional 249 Po Box 39 Km 15 Mem Martins 2726-922T: 00351219269540 F: 00351219269696	Nimed	200 mg	Suppository	Rectal use	Strip	10

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Portugal	Aventis Pharma, Lda. Estrada Nacional 249 Po Box 39 Km 15 Mem Martins 2726-922 T: 00351219269540 F: 00351219269696	Nimed	100mg	Coated Tablet	Oral use	Blister	14; 20; 30 and 60
Portugal	Aventis Pharma, Lda. Estrada Nacional 249 Po Box 39 Km 15 Mem Martins 2726-922 T: 00351219269540 F: 0035121926969	Nimed	100mg	Granules	Oral use	Sachet	14; 20; 30 and 60
Portugal	Aventis Pharma, Lda. Estrada Nacional 249 Po Box 39 Km 15 Mem Martins 2726-922 T: 00351219269540 F: 00351219269696	Nimed Gel	30 mg/g	Gel	Cutaneous use	Tube	30; 50 and 100g
Portugal	Laboratori Guidotti, S.p.A. Via Trieste, 40 56126 Pisa T: 0039050505211 F: 003905040250	Nimesulene	100mg	Granules for oral suspension	Oral use	Sachet	10;20 and 30
Portugal	Clintex - Produtos Farmacêuticos, Lda. Rua João de Deus 19, Venda Nova 2700487 Amadora T.00351214998933 F: 00351214998932	Nimesulida	100mg	Granules for oral suspension	Oral use	Sachet	10; 20; 30 and 60
Portugal	Clintex - Produtos Farmacêuticos, Lda. Rua João de Deus 19, Venda Nova 2700487 Amadora T.00351214998933 F: 00351214998932	Nimesulida Clintex	200 mg	Suppository	Rectal use	Strip	10
Portugal	Clintex - Produtos Farmacêuticos, Lda. Rua João de Deus 19, Venda Nova 2700487 Amadora T.00351214998933 F: 00351214998932	Nimesulida Clintex	100mg	Tablet	Oral use	Blister	10; 20; 30 and 60
Portugal	Angelini Farmacêutica, Lda. - Rua João Chagas n. 53, 3° Piso 1495-072 Algés- Portugal T: 00351214148300 F: 00351214142981	Nimesulide HPF	200mg	Suppository	Rectal use	Strip	12
Portugal	Angelini Farmacêutica, Lda. - Rua João Chagas n. 53 3° Piso 1495-072 Algés- Portugal T: 00351214148300 F: 00351214142981	Nimesulide HPF	100mg	Granules for oral suspension	Oral use	Sachet	14, 30, 60
Portugal	Angelini Farmacêutica, Lda. - Rua João Chagas n. 53 3° Piso 1495-072 Algés- Portugal T: 00351214148300 F: 00351214142981	Nimesulide HPF	100mg	Tablet	Oral use	Blister	14, 30, 60
Portugal	Angelini Farmacêutica, Lda. - Rua João Chagas n. 53	Nimesulide HPF Gel	30 mg/g	Gel	Cutaneous use	Tube	30, 50 and 100g

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
	3° Piso 1495-072 Algés- Portugal T: 00351214148300 F: 00351214142981						

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros T: 00351232831100 F: 00351232831112 Alda Rodrigues - labesfal@mail.telepac.pt	Nimesulida Labesfal	100mg	Granulado para suspensão oral	Via oral	Saqueta	10, 30 e, 60
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros T: 00351232831100 F: 00351232831112 Alda Rodrigues - labesfal@mail.telepac.pt	Nimesulida Labesfal	200 mg	Supositórios	Via rectal	Fita contentora	10
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros T: 00351232831100 F: 00351232831112 Alda Rodrigues - labesfal@mail.telepac.pt	Nimesulida Labesfal	100 mg	Comprimidos	Via oral	Blister	10, 20, 30 e 60
Portugal	Mepha, Investigação , Desenvolvimento e Fabricação LDA Rua Elias Garcia, n.º 28 - C, Apart. 6617-2701-355 Amadora T: 00351 21 476 75 50 - F: 00351214763667	Polyfen	100mg	Tablet	Oral use	Blister	10, 20; 30 and 60
Portugal	Mepha, Investigação , Desenvolvimento e Fabricação LDA Rua Elias Garcia, n.º 28 - C, Apart. 6617-2701-355 Amadora T: 00351 21 476 75 50 - F: 00351214763667	Polyfen	100mg	Granules for oral suspension	Oral use	Sachet	10, 20; 30 and 60
Portugal	Mepha, Investigação , Desenvolvimento e Fabricação LDA Rua Elias Garcia, n.º 28 - C, Apart. 6617-2701-355 Amadora T: 00351 21 476 75 50 - F: 00351214763667	Polyfen	200mg	Suppository	Rectal use	Strip	10
Portugal	Mepha, Investigação , Desenvolvimento e Fabricação LDA Rua Elias Garcia, n.º 28 - C, Apart. 6617-2701-355 Amadora T: 00351 21 476 75 50 - F: 00351214763667	Pronidal - 100	100mg	Tablet	Oral use	Blister	10, 20; 30 and 60

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Portugal	Mepha, Investigação , Desenvolvimento e Fabricação LDA Rua Elias Garcia, n.º 28 - C, Apart. 6617-2701-355 Amadora T: 00351 21 476 75 50 - F: 00351214763667	Pronidal - 100	100mg	Granules for oral suspension	Oral use	Sachet	10, 20; 30 and 60
Portugal	Mepha, Investigação , Desenvolvimento e Fabricação LDA Rua Elias Garcia, n.º 28 - C, Apart. 6617-2701-355 Amadora T: 00351 21 476 75 50 - F: 00351214763667tsalsa@mepha.pt	Pronidal - 200	200 mg	Suppository	Rectal use	Strip	10
Portugal	Farmácia Nova Rua Elias Garcia 10-G Venda Nova 2700 Amadora T: 00351 2638 56800 F: 0351263855020/1 Ms Elsa maria Erminda adm@atral.pt	Ribantil	100mg	Coated Tablet	Oral use	Blister	10; 20; 30 and 60
Portugal	Laboratórios Inibsa, S.A. Apartado 24 Rua do Cotão Velho, S. Marcos Cacém 2735-501 Head office: Sintra Business Park- Zona Industrial da Abrunheira –Edifício 1-2° I/ 2710 089 Sintra T: 00351 21 911 27 30 - F: 00351 21 911 20 23	Sulimed	100mg	Tablet	Oral use	Blister	10; 30 and 60
Portugal	Pentafarma – Sociedade Técnico Medicinal, S.ª Rua Prof. Henrique de Barros, Edif.Sagres, 3rd Piso A – 2685 338 Prior Velho T: 00351 21 942 3672 Fax. 00351 21 942 4043 Ana Real Augusto Filipe tecnimedicina@mail.telepac.pt	Sulinime	100 mg	Tablet	Oral use	Blister	10 ;12 ;20 ; 30; 60

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Portugal	Pentafarma - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros, Edif. Sagres, 3rd Piso A 2685 338 Prior Velho T: 00351219423672 - Fax. 00351219424043	Sulinime	100mg	Granules	Oral use	Sachet	10; 12; 20; 30 and 60
Portugal	Laboratórios Vitória, SA Rua Elias Garcia nº 28, Venda Nova Amadora 2700-327 T: +35121475 83 00 - F: +351214747070 Dina Caldeira - Elisabete Goncalves Dina.c@labvitoria.pt	Vitolide	100mg	Tablet	Oral use	Blister	10 and 30
Portugal	Jabafarma Produtos Farmacêuticos, S.A.Apartado 165 - Zona Industrial da Abrunheira PT- 2711 Sintra T: 00351214329648 F:00351219151930 Head office: rua da tapada grande, 2 Zona Industrial da Abrunheira 2710 089 Sintra Maria Joao Marruz - Julio Carvalhal Maria-marruz@jaba.pt	Zulide	100mg	Tablet	Oral use	Blister	10, 30 and 60
Portugal	Jabafarma Produtos Farmacêuticos, S.A.Apartado 165 - Zona Industrial da Abrunheira PT- 2711 Sintra T: 00351214329648 F:00351219151930 Head office: rua da tapada grande, 2 Zona Industrial da Abrunheira 2710 089 Sintra Maria Joao Marruz - Julio Carvalhal Maria-marruz@jaba.pt	Zulide	100 mg	Granules for oral solution	Oral use	Sachets	10, 30 and 60
Spain	Alcala Farma S.L. CTRA.M-300, Km. 29.902 - E- 28802 Alcala de Henares Madrid- Espana Tel. ++34 91 88 90 600 - Fax. +34 91 889 05 02	Guaxan	100 mg	Granules	Oral use	Sachet	30, 500

Member State	Marketing Authorisation Holder (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Spain	Alcala Farma S.L. CTRA.M-300, Km. 29.902 - E- 28802 Alcala de Henares Madrid- Espana Tel. ++34 91 88 90 600 - Fax. +34 91 889 05 02	Guaxan	100 mg	Tablet	Oral use	Blister	30, 500
Spain	Laboratorios Alter S.A. Mateo Inurria, 30 - E-28036 Madrid Espana Tel. +34 91 35 92 000 - Fax. +34 91 35 01 165	Antifloxil	100 mg	Tablet	Oral use	Blister	30
Spain	Laboratorios Alter S.A. Mateo Inurria, 30 - E-28036 Madrid Espana Tel. +34 91 35 92 000 - Fax. +34 91 35 01 165	Antifloxil	100 mg	Granules	Oral use	Sachet	30

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Belgium	P.S.I. N.V. KRAANLEI 27-29 9000 GENT Tel. +32 9233 1404 Fax. +32 92 33 00 16	NIMESULIDE/SI 100 mg ZAKJES	100 mg	Granules for oral suspension	Oral use	Sachet	30
Belgium	P.S.I. N.V. KRAANLEI 27-29 9000 GENT Tel. +32 9233 1404 Fax. +32 92 33 00 16	NIMESULIDE/ SI 100 mg Tabletten	100 mg	Tablet	Oral use	Blister	

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
France	Laboratoires Arrow Generiques 66, cours Charlemagne 69286 Lyon Cedex 02 FRANCE Tel. +33 4 78 38 53 10 - Fax :+33 4 78 37 52 93 Anne-Sophie Garcia	Nimesulide Arrow	100 mg	Tablet	Oral use	Blister	

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
France	Merck Generiques 34, rue Saint-Romain - 69 359 Lyon Cedex 08 Tel. +33 4 72 78 27 35 -Fax.+33 4 72 78 26 27 ouardia.messili@merckgeneriques.fr delphine.besse@merckgeneriques.fr	Nimesulide Merck	100 mg	Tablet	Oral use	Blister	

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Rafarm Aebe Kirinthou 12 - 15451, N. Psyhiko Tel. +30 10 677 65 50/ Fax. +30 10 677 65 52	Ventor	50 mg/ 5 ml	Oral Suspension	Oral use	Sachet	

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Kleva Epe L. Parnithos 189- Aharne Attikis Tel. +30 210 240 24 05 / Fax. +30 210 24 60 206	Elinap	3 %	Cream	Cutaneous use	Tube	
Greece	Kleva Epe L. Parnithos 189- Aharne Attikis G- 13671 Tel. +30 210 240 24 05 / Fax. +30 210 24 60 206	Elinap	3 %	Gel	Cutaneous use	Tube	

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Pharmacypria Hellas Paster 6 - Ampelokipoi G - 11521 Tel. +30 210 6443132/ Fax. +30 10 644 5375 Ms Sarikaki : pharmcy2@otenet.gr	Lalide	100 mg/ 5ml	Oral Suspension	Oral use	Sachet	
Greece	Pharmacypria Hellas Paster 6- Ampelokipoi G - 11521 Tel. +30 10 65 13 436- Fax. 30 10 644 5375	Lalide	3 %	Gel	Cutaneous use	Tube	30g;50g; 100g.

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Leovan M. Aedn & Cia EE 22, Argonayton Str. Argyroupoli T.K. 164 52 Athens Tel. +30 210 96 04 909 - Fax. +30 210 960 30 95	Lasazin	100 mg	Tablet	Oral use	Blister	2X10 3X10

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Pharmachem Epe Imitou 73 - Vrilissia Attikis - G - 15235 Tel. +30 210 524 74 08/ Fax. +30 210 5244847	Nimesulide Pharmakem	100 mg	Tablet	Oral use	Blister	

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Antonios Polixronis Tou Marinou Thivon 3 / G-15562 Holargos/ Greece Tel. +30 210 65 42 360/ Fax. +30 210 6561006	Omnibus	100 mg	Tablet	Oral use	Blister	1X20 1X30

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Zwitter Pharmaceuticals Ltd. L. Pentelis 34-36 - Athens Greece G-15234 Tel. +30 210 6821098/ Fax.. +30 210 6821098 zwitter@hol.gr	Rhemid	100 mg	Tablet	Oral use	Blister	1X20 1X30

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Med-One S.A. 211 Parnithos Avenue - G-13671 Acharnai - Attiki Tel. +30 210240 24 05/ Fax. +30 2102 46 02 06 Polydefkidoy Eleni	Algosulid	3 %	Cream	Cutaneous use	Tube	
Greece	Med-One S.A. 211 Parnithos Avenue - G-13671 Acharnai - Attiki Tel. +30 210240 24 05/ Fax. +30 2102 46 02 06 Polydefkidoy Eleni	Algosulid	100 mg	Tablet	Oral use	Blister	

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Lamda Pharmaceutical AE 6, Thermopylon Str/ G-15233 Halandri - Athens Tel. +30 210 68 56 741 –2/ Fax. +30 210 68 46 829 Stefania Staikou - Vaggelis Karras info@lamdapharmaceuticals.gr	Nimesoral	50 mg/ 5ml	Oral Suspension	Oral use	Bottle	1X100ml
Greece	Lamda Pharmaceutical AE 6, Thermopylon Str/ G-15233 Halandri - Athens Tel. +30 210 68 56 741 –2/ Fax. +30 210 68 46 829 Stefania Staikou / Vaggelis Karras info@lamdapharmaceuticals.gr	Nimegel	3 %	Gel	Cutaneous use	Tube	1x30g 1x50g 1x100g

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Medicon Pharmaceutical S.A. Karaiskaki 115°A/ G-26500 Aktaio –Rio Patron Greece Tel.: +30 6932200188 - Fax. +30 2610 99 38 08 chrodopoulos@yahoo.gr	Nimesulide Medicon	100 mg	Tablet	Oral use	Blister	2x10 3x10

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Greece	Farmamust Epe Plateia Pantazopoulou 7/ G-10443 Kolonos Attikis	Lovirem	100 mg	Tablet	Oral use	Blister	

Member State	Applicant (Name, address, phone and fax numbers)	Invented Name	Strength	Pharmaceutical Form	Route of administration	Packaging	Pack Size
Spain	Laboratorios Alcala Farma S.L.Ctra. M-300, Km. 29,920 E-28802 Alcala' de Henares (Madrid) Tel. +34 91 889 06 00 - Fax. +34 91 889 05 02	Guaxan Gel	3 g/ 100 g	Gel	Topic use	Tube	30 50 100 g

ANNEX II

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

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF NIMESULIDE CONTAINING MEDICINAL PRODUCTS

Nimesulide is a non-steroidal anti-inflammatory drug (NSAID).
Nimesulide containing medicinal products are currently marketed in more than 50 countries world-wide. In Europe, nimesulide is nationally authorised in 10 Member States: Austria, Belgium, Finland, France, Greece, Ireland, Italy, Luxembourg, Portugal and Spain. The first launch was in Italy in 1985.
The multitude of national Marketing Authorisations granted at different points in time has lead to divergence in the approved therapeutic indications, posology, recommended duration of treatment in the European Community.

Following the granting of marketing authorisation of nimesulide products in Finland (January 1998), cases of hepatic adverse reactions, ranging from asymptomatic increases in liver enzymes to hepatic failure that required liver transplant, have been reported. By 13 March 2002, the Finnish National Agency for Medicines had received altogether 109 Adverse Drug Reaction reports concerning nimesulide, of these 66 were hepatic reactions, including serious reactions (e.g. hepatitis, hepatic failure, including two cases necessitating liver transplantation). Based on these serious hepatic reactions and taking into account the relatively non-serious conditions for which nimesulide is indicated for as well as the existence of numerous alternative treatments, the Marketing Authorisations of nimesulide containing medicinal products for oral administration have been suspended in Finland on 18 March 2002.

On 10 April 2002, Finland notified the CPMP and EMEA Secretariat of a referral under Article 31 of Directive 2001/83/EC as amended, requesting the CPMP to give its opinion on the risk-benefit balance of all nimesulide containing medicinal products, especially in view of the hepatic toxicity.

Furthermore, on 3 May 2002, Spain circulated a Rapid Alert about the suspension of the marketing of nimesulide containing medicinal products in their territory.

EFFICACY

Nimesulide has been shown to be effective in **acute pain**, **primary dysmenorrhoea** and in the **symptomatic treatment of painful osteoarthritis** for the systemic formulations.

Nimesulide has been shown to be effective in **symptomatic relief of pain associated with sprains and acute traumatic tendinitis** for the topical formulations**.**

SAFETY

For NSAIDs, the most common adverse events are **gastro-intestinal** reactions, with dyspepsia and other non-serious complaints, but also ulcers, bleeding, and perforation, which can be very severe and even fatal.
Examining the safety data from clinical trials and pharmacoepidemiological data comparing nimesulide with other NSAIDs such as meloxicam, diclofenac and ibuprofen, nimesulide has shown to have a comparable gastrointestinal safety profile especially after short-term treatment.

Renal reactions appear to be a very rare event for nimesulide.

Data from two independent spontaneous ADR reporting systems in Finland and in Spain suggest that nimesulide has an increase risk of **hepatoxicity** compared to other NSAIDs. However, this finding was not confirmed in any other EU Member States where nimesulide has been marketed. The reasons for such difference in reporting rates among Member States is unclear. A pharmacoepidemiology study suggests a slightly increased risk of hepatic reactions with nimesulide compared to the group of other NSAIDs analysed as a whole.

Overall, based on the assessment of world-wide post-marketing spontaneous reporting systems, clinical trials, and epidemiological data, the frequency of severe adverse hepatic reactions with nimesulide appears to be similar to many other NSAIDs.

Nimesulide appears to be also similar to the other NSAIDs as regards its overall safety profile, including gastrointestinal and renal undesirable effects.

MODIFICATION OF THE PRODUCT INFORMATION

The CPMP decided to restrict the use of nimesulide to the indications of treatment of acute pain, symptomatic treatment of osteoarthritis and primary dysmenorrhoea for the systemic formulations and symptomatic relief of pain associated with sprains and acute traumatic tendinitis for the topical formulations.

The maximum nimesulide daily dose should be 100 mg bid orally, and the treatment should be for the shortest possible duration.
In accordance with the assessment of the efficacy data submitted by the MAHs/Applicants and the CPMP recommendations on the maximum nimesulide daily dose of 100 mg bid orally, the MAHs have withdrawn all Marketing Authorisations for the 200 mg tablet strength.

CONCLUSION

The CPMP considered that the risk-benefit profile of nimesulide containing products for systemic and topical use is favourable and that Marketing Authorisations, except for the 200mg tablets, should be maintained/granted with the following restrictions:

1. The Summaries of Products Characteristics as set out in Annex III of the CPMP Opinion
2. The CPMP requirements set out in Annex IV of the CPMP Opinion:
    - 6-monthly Periodic Safety Update Report should be provided to the National Authorities. Such report should include a specific overview on hepatic reactions and on the relationship between hepatic reactions and potential risk factors such as age >65, gender, co-administration of other medicinal products. In each of the PSURs, all hepatic ADRs should be reviewed in detail.
- The MAHs should inform the public of the finalisation of the referral and of the revised conditions of nimesulide use. This information should be done via a Dear Doctor Letter (DDL), to be agreed in due time with the National Authorities so its distribution coincides with the Commission Decision on this issue.

In accordance with the assessment of the efficacy data provided by the MAHs/Applicants and with the CPMP recommendations on the maximum daily oral posology of 100 mg bid, the CPMP concludes that the efficacy of the oral dosage of 200mg twice-a-day is not supported; in consequence the Marketing Authorisations for the 200 mg tablets have to be withdrawn and Marketing Authorisations of the 200mg tablet should not be granted.

ANNEX III

SUMMARIES OF PRODUCT CHARACTERISTICS

SUMMARY OF PRODUCT CHARACTERISTICS

NIMESULIDE 100 MG TABLETS, SOLUBLE TABLETS, EFFERVESCENT TABLETS, COATED TABLETS, CAPSULES, HARD CAPSULES,
NIMESULIDE 50/100 MG GRANULES OR POWDER FOR ORAL SUSPENSION
NIMESULIDE 1%, 2% OR 5% ORAL SUSPENSION

1. NAME OF THE MEDICINAL PRODUCT

<TRADENAME>

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet, soluble tablet, effervescent tablet, coated tablet, capsule, hard capsule contains 100mg nimesulide.
Each sachet contains 50 or 100mg nimesulide.
Oral suspension containing 10mg, 20mg or 50mg per ml.

For excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet, soluble tablet, effervescent tablet or coated tablet: <Company-specific>
Granules or powder for oral suspension: <Company-specific>
Capsule, hard capsule: <Company-specific>
Oral suspension: <Company-specific>

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of acute pain.
Symptomatic treatment of painful osteoarthritis.
Primary dysmenorrhoea.

4.2 Posology and method of administration

<Nimesulide-containing medicinal products> should be used for the shortest possible duration, as required by the clinical situation.

Adults**:**
100mg nimesulide tablets, soluble tablets, effervescent tablets, coated tablets, capsules, hard capsules, 50mg and 100mg granules or powder, 1%, 2% and 5% oral suspension: 100mg bid after meal

Elderly: in elderly patients there is no need to reduce the daily dosage (see section 5.2).

Children (< 12 years): <Nimesulide containing medicinal products> are contraindicated in these patients (see also section 4.3).

Adolescents (from 12 to 18 years): on the basis of the kinetic profile in adults and on the pharmacodynamic characteristics of nimesulide, no dosage adjustment in these patients is necessary.

Impaired renal function: on the basis of pharmacokinetics, no dosage adjustment is necessary in patients with mild to moderate renal impairment (creatinine clearance of 30-80 ml/min), while <Nimesulide containing medicinal products> are contraindicated in case of severe renal impairement (creatinine clearance < 30ml/min) (see sections 4.3 and 5.2).

Hepatic impairment: the use of <Nimesulide containing medicinal products> is contraindicated in patients with hepatic impairment (see section 5.2).

4.3 Contraindications

Known hypersensitivity to nimesulide or to any of the excipients of the products.
History of hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria) in response to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs.
History of hepatotoxic reactions to nimesulide
Active gastric or duodenal ulcer, a history of recurrent ulceration or gastrointestinal bleeding, cerebrovascular bleeding or other active bleeding or bleeding disorders.
Severe coagulation disorders.
Severe heart failure
Severe renal impairment.
Hepatic impairment.
Children under 12 years.
The third trimester of pregnancy and breastfeeding (see sections 4.6 and 5.3).

4.4 Special warnings and special precautions for use

The risk of undesirable effects may be reduced by using <Nimesulide- containing medicinal products> for the shortest possible duration.
Treatment should be discontinued if no benefit is seen.

Rarely <Nimesulide-containing medicinal products> have been reported to be associated with serious hepatic reactions, including very rare fatal cases (see also section 4.8). Patients who experience symptoms compatible with hepatic injury during treatment with <Nimesulide-containing medicinal products> (e.g. anorexia, nausea, vomiting, abdominal pain, fatigue, dark urine) or patients who develop abnormal liver function tests should have treatment discontinued. These patients should not be rechallenged with nimesulide. Liver damage, in most cases reversible, has been reported following short exposure to the drug.

Concomitant administration with known hepatotoxic drugs, and alcohol abuse must be avoided during treatment with <Nimesulide-containing medicinal products> treatment, since either may increase the risk of hepatic reactions.

During therapy with <Nimesulide-containing medicinal products>, patients should be advised to refrain from other analgesics. Simultaneous use of different NSAIDs is not recommended.

Gastrointestinal bleeding or ulceration / perforation can occur at any time during treatment with or without warning symptoms or a previous history of gastrointestinal events. If gastrointestinal bleeding or ulceration occurs, nimesulide should be discontinued. Nimesulide should be used with caution in patients with gastrointestinal disorders, including history of peptic ulceration, history of gastrointestinal haemorrhage, ulcerative colitis or Crohn's disease.

In patients with renal or cardiac impairment, caution is required since the use of <Nimesulide-containing medicinal products> may result in deterioration of renal function. In the event of deterioration, the treatment should be discontinued (see also section 4.5).

Elderly patients are particularly susceptible to the adverse effects of NSAIDs, including gastrointestinal haemorrhage and perforation, impaired renal, cardiac and hepatic function. Therefore, appropriate clinical monitoring is advisable.

As nimesulide can interfere with platelet function, it should be used with caution in patients with bleeding diathesis (see also section 4.3). However, <Nimesulide-containing medicinal products> is not a substitute for acetylsalicylic acid for cardiovascular prophylaxis.

NSAIDs may mask the fever related to an underlying bacterial infection.

The use of <Nimesulide-containing medicinal products> may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of <Nimesulide-containing medicinal products> should be considered (see section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions
Patients receiving warfarin or similar anticoagulant agents or acetylsalicylic acid have an increased risk of bleeding complications, when treated with <Nimesulide-containing medicinal products>. Therefore this combination is not recommended (see also section 4.4.) and is contraindicated in patients with severe coagulation disorders (see also section 4.3). If the combination cannot be avoided, anticoagulant activity should be monitored closely.

Pharmacodynamic/pharmacokinetic interactions with diuretics
In healthy subjects, nimesulide transiently decreases the effect of furosemide on sodium excretion and, to a lesser extent, on potassium excretion and reduces the diuretic response.
Co-administration of nimesulide and furosemide results in a decrease (of about 20%) of the AUC and cumulative excretion of furosemide, without affecting its renal clearance.
The concomitant use of furosemide and <Nimesulide containing medicinal products> requires caution in susceptible renal or cardiac patients, as described under section 4.4.

Pharmacokinetic interactions with other drugs:
Non-steroidal anti-inflammatory drugs have been reported to reduce the clearance of lithium, resulting in elevated plasma levels and lithium toxicity. If <Nimesulide containing medicinal products> are prescribed for a patient receiving lithium therapy, lithium levels should be monitored closely.

Potential pharmacokinetic interactions with glibenclamide, theophylline, warfarin, digoxin, cimetidine and an antacid preparation (i.e. a combination of aluminium and magnesium hydroxide) were also studied in vivo. No clinically significant interactions were observed.

Nimesulide inhibits CYP2C9. The plasma concentrations of drugs that are substrates of this enzyme may be increased when <Nimesulide containing medicinal products> are used concomitantly.

Caution is required if nimesulide is used less than 24 hours before or after treatment with methotrexate because the serum level of methotrexate might increase and therefore, the toxicity of this drug might increase.
Due to their effect on renal prostaglandines, prostaglandin synthetase inhibitors like nimesulide may increase the nephrotoxicity of cyclosporines.

Effects of other drugs on nimesulide:
In vitro studies have shown displacement of nimesulide from binding sites by tolbutamide, salicylic acid and valproic acid. However, despite a possible effect on plasma levels, these interactions have not demonstrated clinical significance.

4.6 Pregnancy and lactation

The use of <Nimesulide containing medicinal products> is contraindicated in the third trimester of pregnancy (see section 4.3).
Like other NSAIDs <Nimesulide containing medicinal products> is not recommended in women attempting to conceive (see section 4.4). As with other NSAIDs, known to inhibit prostaglandin synthesis, nimesulide may cause premature closure of the ductus arteriosus, pulmonary hypertension, oliguria, oligoamnios, increased risk of bleeding, uterine inertia and peripheral oedema. There have been isolated reports of renal failure in neonates born to women taking nimesulide in late pregnancy.

Studies in rabbits have shown an atypical reproductive toxicity (see section 5.3) and no adequate data from the use of nimesulide-containing medicinal products in pregnant women are available. Therefore, the potential risk for humans is unknown and prescribing the drug during the first two trimesters of pregnancy is not recommended.

Lactation:
It is not known whether nimesulide is excreted in human milk. <Nimesulide containing medicinal products> are contraindicated when breastfeeding (see sections 4.3 and 5.3).

4.7 Effects on ability to drive and use machines

No studies on the effect of <Nimesulide containing medicinal products> on the ability to drive or use machines have been performed. However, patients who experience dizziness, vertigo or somnolence after receiving <Nimesulide containing medicinal products> should refrain from driving or operating machines.

4.8 Undesirable effects

The following listing of undesirable effects is based on data from controlled clinical trials* (approximately 7,800 patients) and from post marketing surveillance with reporting rates classified as: very common (>1/10); common (>1/100, <1/10), uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000), including isolated cases.

Blood disorders	Rare	Anaemia* Eosinophilia*
	Very rare	Thrombocytopenia Pancytopenia Purpura
Immune system disorders	Rare	Hypersensitivity*
	Very rare	Anaphylaxis
Metabolism and nutrition disorders	Rare	Hyperkalaemia*
Psychiatric disorders	Rare	Anxiety* Nervousness* Nightmare*
Nervous system disorders	Uncommon	Dizziness*
	Very rare	Headache Somnolence Encephalopathy (Reye's syndrome)
Eye disorders	Rare	Vision blurred*
	Very rare	Visual disturbance
Ear and labyrinth disorders	Very rare	Vertigo
Cardiac disorders	Rare	Tachycardia*
Vascular disorders	Uncommon	Hypertension*
	Rare	Haemorrhage* Blood pressure fluctuation* Hot flushes*
Respiratory disorders	Uncommon	Dyspnoea*
	Very rare	Asthma Bronchospasm
Gastrointestinal disorders	Common	Diarrhoea* Nausea* Vomiting*
	Uncommon	Constipation* Flatulence* Gastritis*

	Very rare	Abdominal pain Dyspepsia Stomatitis Melaena Gastrointestinal bleeding Duodenal ulcer and perforation Gastric ulcer and perforation
Hepato-biliary disorders (see section 4.4."Special warnings and special precautions for use")	Very rare	Hepatitis Fulminant hepatitis (including fatal cases) Jaundice Cholestasis
Skin and subcutaneous tissue disorders	Uncommon	Pruritus* Rash* Sweating increased*
	Rare	Erythema* Dermatitis*
	Very rare	Urticaria Angioneurotic oedema Face oedema Erythema multiforme Stevens Johnson syndrome Toxic epidermal necrolysis
Renal and urinary disorders	Rare	Dysuria* Haematuria* Urinary retention*
	Very rare	Renal failure Oliguria Interstitial nephritis
General disorders	Uncommon	Oedema*
	Rare	Malaise* Asthenia*
	Very rare	Hypothermia
Investigations	Common	Hepatic enzymes increased*
*frequency based on clinical trial		

4.9 Overdose

Symptoms following acute NSAID overdoses are usually limited to lethargy, drowsiness, nausea, vomiting and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.
Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. No information is available regarding the removal of nimesulide by haemodialysis, but based on its high degree of plasma protein binding (up to 97.5%) dialysis is unlikely to be useful in overdose. Emesis and/or activated charcoal (60 to 100 g in adults) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose. Forced diuresis, alkalinization of urine, haemodialysis, or haemoperfusion may not be useful due to high protein binding. Renal and hepatic function should be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
ATC code: M01AX17

Nimesulide is a non-steroidal anti-inflammatory drug with analgesic and antipyretic properties which acts as an inhibitor of prostaglandin synthesis enzyme cyclo-oxygenase.

5.2 Pharmacokinetic properties

Nimesulide is well absorbed when given by mouth. After a single dose of 100mg nimesulide a peak plasma level of 3-4 mg/l is reached in adults after 2-3 hours. AUC = 20 - 35 mg h/l. No statistically significant difference has been found between these figures and those seen after 100mg given twice daily for 7 days.

Up to 97.5% binds to plasma proteins**.**

Nimesulide is extensively metabolised in the liver following multiple pathways, including cytochrome P450 (CYP) 2C9 isoenzymes. Therefore, there is the potential for a drug interaction with concomitant administration of drugs which are metabolised by CYP2C9 (see under section 4.5). The main metabolite is the para-hydroxy derivative which is also pharmacologically active. The lag time before the appearance of this metabolite in the circulation is short (about 0.8 hour) but its formation constant is not high and is considerably lower than the absorption constant of nimesulide. Hydroxynimesulide is the only metabolite found in plasma and it is almost completely conjugated. $T_{½}$ is between 3.2 and 6 hours.

Nimesulide is excreted mainly in the urine (approximately 50% of the administered dose).
Only 1-3% is excreted as the unmodified compound. Hydroxynimesulide, the main metabolite is found only as a glucuronate. Approximately 29% of the dose is excreted after metabolism in the faeces.

The kinetic profile of nimesulide was unchanged in the elderly after acute and repeated doses.

In an acute experimental study carried out in patients with mild to moderate renal impairment (creatinine clearance 30-80 ml/min) versus healthy volunteers, peak plasma levels of nimesulide and its main metabolite were not higher than in healthy volunteers. AUC and t1/2 beta were 50% higher, but where always within the range of kinetic values observed with nimesulide in healthy volunteers. Repeated administration did not cause accumulation.
Nimesulide is contra-indicated in patients with hepatic impairment (see section 4.3).

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.
In repeated dose toxicity studies, nimesulide showed gastrointestinal, renal and hepatic toxicity.
In reproductive toxicity studies, embryotoxic and teratogenic effects (skeletal malformations, dilatation of cerebral ventricles) were observed in rabbits, but not in rats, at maternally non-toxic dose levels. In rats, increased mortality of offspring was observed in the early postnatal period and nimesulide showed adverse effects on fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients
6.2 Incompatibilities

6.3 Shelf life

6.4 Special precautions for storage

6.5 Nature and contents of the container

6.6 Instructions for use/handling

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTORISATION NUMBER

9. DATE OF FIRST AUTHORISATION /RENEWAL OF AUTHORISATION

10. DATE OF (PARTIAL) REVISION OF THE TEXT

SUMMARY OF PRODUCT CHARACTERISTICS

NIMESULIDE-β-CYCLODEXTRIN 400 MG
TABLETS AND GRANULES FOR ORAL SUSPENSION

1. NAME OF THE MEDICINAL PRODUCT

<TRADENAME>

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each sachet and tablet contains 400mg nimesulide-β-cyclodextrin, corresponding to 100mg nimesulide.

For excipients, see section 6.1

3. PHARMACEUTICAL FORM

Tablet: <Company-specific>Granules for oral suspension: <Company-specific>.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of acute pain.
Symptomatic treatment of painful osteoarthritis.
Primary dysmenorrhoea.

4.2 Posology and method of administration

<Nimesulide-containing medicinal products> should be used for the shortest possible duration, as required by the clinical situation.

Adults**:**
400mg nimesulide-β-cyclodextrin sachet and tablet (=100mg nimesulide) bid after meal.

Elderly: in elderly patients there is no need to reduce the daily dosage (see section 5.2).

Children (< 12 years): <Nimesulide containing medicinal products> are contraindicated in these patients (see also section 4.3).

Adolescents (from 12 to 18 years): on the basis of the kinetic profile in adults and on the pharmacodynamic characteristics of nimesulide, no dosage adjustment in these patients is necessary.

Impaired renal function: on the basis of pharmacokinetics, no dosage adjustment is necessary in patients with mild to moderate renal impairment (creatinine clearance of 30-80 ml/min), while <Nimesulide containing medicinal products> are contraindicated in case of severe renal impairement (creatinine clearance < 30ml/min) (see sections 4.3 and 5.2).

Hepatic impairment: the use of <Nimesulide containing medicinal products> is contraindicated in patients with hepatic impairment (see section 5.2).

4.3 Contraindications

Known hypersensitivity to nimesulide or to any of the excipients of the products.
History of hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria) in response to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs.

History of hepatotoxic reactions to nimesulide
Active gastric or duodenal ulcer, a history of recurrent ulceration or gastrointestinal bleeding, cerebrovascular bleeding or other active bleeding or bleeding disorders.
Severe coagulation disorders.
Severe heart failure
Severe renal impairment.
Hepatic impairment.
Children under 12 years.
The third trimester of pregnancy and breastfeeding (see sections 4.6 and 5.3).

4.4 Special warnings and special precautions for use

The risk of undesirable effects may be reduced by using <Nimesulide- containing medicinal products> for the shortest possible duration.
Treatment should be discontinued if no benefit is seen.

Rarely <Nimesulide-containing medicinal products> have been reported to be associated with serious hepatic reactions, including very rare fatal cases (see also section 4.8). Patients who experience symptoms compatible with hepatic injury during treatment with <Nimesulide-containing medicinal products> (e.g. anorexia, nausea, vomiting, abdominal pain, fatigue, dark urine) or patients who develop abnormal liver function tests should have treatment discontinued. These patients should not be rechallenged with nimesulide. Liver damage, in most cases reversible, has been reported following short exposure to the drug.

Concomitant administration with known hepatotoxic drugs, and alcohol abuse must be avoided during treatment with <Nimesulide-containing medicinal products>, since either may increase the risk of hepatic reactions.

During therapy with <Nimesulide-containing medicinal products>, patients should be advised to refrain from other analgesics. Simultaneous use of different NSAIDs is not recommended.

Gastrointestinal bleeding or ulceration / perforation can occur at any time during treatment with or without warning symptoms or a previous history of gastrointestinal events. If gastrointestinal bleeding or ulceration occurs, nimesulide should be discontinued. Nimesulide should be used with caution in patients with gastrointestinal disorders, including history of peptic ulceration, history of gastrointestinal haemorrhage, ulcerative colitis or Crohn's disease.

In patients with renal or cardiac impairment, caution is required since the use of <Nimesulide-containing medicinal products> may result in deterioration of renal function. In the event of deterioration, the treatment should be discontinued (see also section 4.5).

Elderly patients are particularly susceptible to the adverse effects of NSAIDs, including gastrointestinal haemorrhage and perforation, impaired renal, cardiac and hepatic function. Therefore, appropriate clinical monitoring is advisable.

As nimesulide can interfere with platelet function, it should be used with caution in patients with bleeding diathesis (see also section 4.3). However, <Nimesulide-containing medicinal products> is not a substitute for acetylsalicylic acid for cardiovascular prophylaxis.

NSAIDs may mask the fever related to an underlying bacterial infection.

The use of <Nimesulide-containing medicinal products> may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of <Nimesulide-containing medicinal products> should be considered (see section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions
Patients receiving warfarin or similar anticoagulant agents or acetylsalicylic acid have an increased risk of bleeding complications, when treated with <Nimesulide-containing medicinal products>. Therefore this combination is not recommended (see also section 4.4.) and is contraindicated in patients with severe coagulation disorders (see also section 4.3). If the combination cannot be avoided, anticoagulant activity should be monitored closely.

Pharmacodynamic/pharmacokinetic interactions with diuretics
In healthy subjects, nimesulide transiently decreases the effect of furosemide on sodium excretion and, to a lesser extent, on potassium excretion and reduces the diuretic response.
Co-administration of nimesulide and furosemide results in a decrease (of about 20%) of the AUC and cumulative excretion of furosemide, without affecting its renal clearance.
The concomitant use of furosemide and <Nimesulide containing medicinal products> requires caution in susceptible renal or cardiac patients, as described under section 4.4.

Pharmacokinetic interactions with other drugs:
Non-steroidal anti-inflammatory drugs have been reported to reduce the clearance of lithium, resulting in elevated plasma levels and lithium toxicity. If <Nimesulide containing medicinal products> are prescribed for a patient receiving lithium therapy, lithium levels should be monitored closely.

Potential pharmacokinetic interactions with glibenclamide, theophylline, warfarin, digoxin, cimetidine and an antacid preparation (i.e. a combination of aluminium and magnesium hydroxide) were also studied in vivo. No clinically significant interactions were observed.

Nimesulide inhibits CYP2C9. The plasma concentrations of drugs that are substrates of this enzyme may be increased when <Nimesulide containing medicinal products> are used concomitantly.

Caution is required if nimesulide is used less than 24 hours before or after treatment with methotrexate because the serum level of methotrexate might increase and therefore, the toxicity of this drug might increase.
Due to their effect on renal prostaglandines, prostaglandin synthetase inhibitors like nimesulide may increase the nephrotoxicity of cyclosporines.

Effects of other drugs on nimesulide:
In vitro studies have shown displacement of nimesulide from binding sites by tolbutamide, salicylic acid and valproic acid. However, despite a possible effect on plasma levels, these interactions have not demonstrated clinical significance.

4.6 Pregnancy and lactation

The use of <Nimesulide containing medicinal products> is contraindicated in the third trimester of pregnancy (see section 4.3).
Like other NSAIDs, <Nimesulide containing medicinal products> is not recommended in women attempting to conceive (see section 4.4). As with other NSAIDs known to inhibit prostaglandin synthesis, nimesulide may cause premature closure of the ductus arteriosus, pulmonary hypertension, oliguria, oligoamnios, increased risk of bleeding, uterine inertia and peripheral oedema. There have been isolated reports of renal failure in neonates born to women taking nimesulide in late pregnancy.

Studies in rabbits have shown an atypical reproductive toxicity (see section 5.3) and no adequate data from the use of nimesulide-containing medicinal products in pregnant women are available. Therefore, the potential risk for humans is unknown and prescribing the drug during the first two trimesters of pregnancy is not recommended.

Lactation:
It is not known whether nimesulide is excreted in human milk. <Nimesulide containing medicinal products> are contraindicated when breastfeeding (see sections 4.3 and 5.3).

4.7 Effects on ability to drive and use machines

No studies on the effect of <Nimesulide containing medicinal products> on the ability to drive or use machines have been performed. However, patients who experience dizziness, vertigo or somnolence after receiving <Nimesulide containing medicinal products> should refrain from driving or operating machines.

4.8 Undesirable effects

The following listing of undesirable effects is based on data from controlled clinical trials* (approximately 7,800 patients) and from post marketing surveillance with reporting rates classified as very common (>1/10); common (>1/100, <1/10), uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000), including isolated cases.

Blood disorders	Rare	Anaemia* Eosinophilia*
	Very rare	Thrombocytopenia Pancytopenia Purpura
Immune system disorders	Rare	Hypersensitivity*
	Very rare	Anaphylaxis
Metabolism and nutrition disorders	Rare	Hyperkalaemia*
Psychiatric disorders	Rare	Anxiety* Nervousness* Nightmare*
Nervous system disorders	Uncommon	Dizziness*
	Very rare	Headache Somnolence Encephalopathy (Reye's syndrome)
Eye disorders	Rare	Vision blurred*
	Very rare	Visual disturbance
Ear and labyrinth disorders	Very rare	Vertigo
Cardiac disorders	Rare	Tachycardia*
Vascular disorders	Uncommon	Hypertension*
	Rare	Haemorrhage* Blood pressure fluctuation* Hot flushes*
Respiratory disorders	Uncommon	Dyspnoea*
	Very rare	Asthma Bronchospasm
Gastrointestinal disorders	Common	Diarrhoea* Nausea* Vomiting*
	Uncommon	Constipation* Flatulence* Gastritis*

	Very rare	Abdominal pain Dyspepsia Stomatitis Melaena Gastrointestinal bleeding Duodenal ulcer and perforation Gastric ulcer and perforation
Hepato-biliary disorders *(see section 4.4."Special warnings and special precautions for use")*	Very rare	Hepatitis Fulminant hepatitis (including fatal cases) Jaundice Cholestasis
Skin and subcutaneous tissue disorders	Uncommon	Pruritus* Rash* Sweating increased*
	Rare	Erythema* Dermatitis*
	Very rare	Urticaria Angioneurotic oedema Face oedema Erythema multiforme Stevens Johnson syndrome Toxic epidermal necrolysis
Renal and urinary disorders	Rare	Dysuria* Haematuria* Urinary retention*
	Very rare	Renal failure Oliguria Interstitial nephritis
General disorders	Uncommon	Oedema*
	Rare	Malaise* Asthenia*
	Very rare	Hypothermia
Investigations	Common	Hepatic enzymes increased*

**frequency based on clinical trial*

4.9 Overdose

Symptoms following acute NSAID overdoses are usually limited to lethargy, drowsiness, nausea, vomiting and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.

Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. No information is available regarding the removal of nimesulide by haemodialysis, but based on its high degree of plasma protein binding (up to 97.5%) dialysis is unlikely to be useful in overdose. Emesis and/or activated charcoal (60 to 100 g in adults) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose. Forced diuresis, alkalinization of urine, haemodialysis, or haemoperfusion may not be useful due to high protein binding. Renal and hepatic function should be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
ATC code: M01AX17

Nimesulide is a non-steroidal anti-inflammatory drug with analgesic and antipyretic properties which acts as an inhibitor of prostaglandin synthesis enzyme cyclo-oxygenase.

5.2 Pharmacokinetic properties

Nimesulide is well absorbed when given by mouth. After a single dose of 100mg nimesulide a peak plasma level of 3-4 mg/l is reached in adults after 2-3 hours. AUC = 20 - 35 mg h/l. No statistically significant difference has been found between these figures and those seen after 100mg given twice daily for 7 days.

After single doses, nimesulide β-cyclodextrin 400 mg sachets were found bioequivalent to <Nimesulide containing medicinal products> 100 mg sachets, with respect to AUC and Cmax. parameters. Moreover t½ was nearly identical for both formulations, while the Tmax was about 1.5 and 2.5 hrs. respectively for nimesulide β-cyclodextrin sachets and <Nimesulide containing medicinal products> sachets, showing a more rapid absorption of the former.

Up to 97.5% binds to plasma proteins.

Nimesulide is extensively metabolised in the liver following multiple pathways, including cytochrome P450 (CYP) 2C9 isoenzymes. Therefore, there is the potential for a drug interaction with concomitant administration of drugs which are metabolised by CYP2C9 (see under section 4.5). The main metabolite is the para-hydroxy derivative which is also pharmacologically active. The lag time before the appearance of this metabolite in the circulation is short (about 0.8 hour) but its formation constant is not high and is considerably lower than the absorption constant of nimesulide. Hydroxynimesulide is the only metabolite found in plasma and it is almost completely conjugated. $T_{½}$ is between 3.2 and 6 hours.

Nimesulide is excreted mainly in the urine (approximately 50% of the administered dose).
Only 1-3% is excreted as the unmodified compound. Hydroxynimesulide, the main metabolite is found only as a glucuronate. Approximately 29% of the dose is excreted after metabolism in the faeces.

The kinetic profile of nimesulide was unchanged in the elderly after acute and repeated doses.

In an acute experimental study carried out in patients with mild to moderate renal impairment (creatinine clearance 30-80 ml/min) versus healthy volunteers, peak plasma levels of nimesulide and its main metabolite were not higher than in healthy volunteers. AUC and t1/2 beta were 50% higher, but were always within the range of kinetic values observed with nimesulide in healthy volunteers. Repeated administration did not cause accumulation.
Nimesulide is contra-indicated in patients with hepatic impairment (see section 4.3).

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.
In repeated dose toxicity studies, nimesulide showed gastrointestinal, renal and hepatic toxicity.
In reproductive toxicity studies, embryotoxic and teratogenic effects (skeletal malformations, dilatation of cerebral ventricles) were observed in rabbits, but not in rats, at maternally non-toxic dose

levels. In rats, increased mortality of offspring was observed in the early postnatal period and nimesulide showed adverse effects on fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

6.2 Incompatibilities

6.3 Shelf life

6.4 Special precautions for storage

6.5 Nature and contents of the container

6.6 Instructions for use/handling

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTORISATION NUMBER

9. DATE OF FIRST AUTHORISATION /RENEWAL OF AUTHORISATION

10. DATE OF (PARTIAL) REVISION OF THE TEXT

SUMMARY OF PRODUCT CHARACTERISTICS

NIMESULIDE 100 MG OR 200 MG SUPPOSITORIES

1. **NAME OF THE MEDICINAL PRODUCT**

<TRADENAME>

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each suppository contains 100mg or 200mg nimesulide.

For excipients, see section 6.1

3. PHARMACEUTICAL FORM

Suppository: <Company-specific>.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of acute pain.
Symptomatic treatment of painful osteoarthritis.
Primary dysmenorrhoea.

4.2 Posology and method of administration

<Nimesulide-containing medicinal products> should be used for the shortest possible duration, as required by the clinical situation.

Adults**:**
100mg or 200mg nimesulide suppositories: 200mg twice daily

Elderly: in elderly patients there is no need to reduce the daily dosage (see section 5.2).

Children (< 12 years): <Nimesulide containing medicinal products> are contraindicated in these patients (see also section 4.3).

Adolescents (from 12 to 18 years): on the basis of the kinetic profile in adults and on the pharmacodynamic characteristics of nimesulide, no dosage adjustment in these patients is necessary.

Impaired renal function: on the basis of pharmacokinetics, no dosage adjustment is necessary in patients with mild to moderate renal impairment (creatinine clearance of 30-80 ml/min), while <Nimesulide containing medicinal products> are contraindicated in case of severe renal impairement (creatinine clearance < 30ml/min) (see sections 4.3 and 5.2).

Hepatic impairment: the use of <Nimesulide containing medicinal products> is contraindicated in patients with hepatic impairment (see section 5.2).

4.3 Contraindications

Known hypersensitivity to nimesulide or to any of the excipients of the products.
History of hypersensitivity reactions (e.g. bronchospasm, rhinitis, urticaria) in response to acetylsalicylic acid or other non-steroidal anti-inflammatory drugs.
History of hepatotoxic reactions to nimesulide
Active gastric or duodenal ulcer, a history of recurrent ulceration or gastrointestinal bleeding, cerebrovascular bleeding or other active bleeding or bleeding disorders.
Severe coagulation disorders.
Severe heart failure
Severe renal impairment.

Hepatic impairment.
Children under 12 years.
The third trimester of pregnancy and breastfeeding (see sections 4.6 and 5.3).

4.4 Special warnings and special precautions for use

The risk of undesirable effects may be reduced by using <Nimesulide- containing medicinal products> for the shortest possible duration.
Treatment should be discontinued if no benefit is seen.

Rarely <Nimesulide-containing medicinal products> have been reported to be associated with serious hepatic reactions, including very rare fatal cases (see also section 4.8). Patients who experience symptoms compatible with hepatic injury during treatment with <Nimesulide-containing medicinal products> (e.g. anorexia, nausea, vomiting, abdominal pain, fatigue, dark urine) or patients who develop abnormal liver function tests should have treatment discontinued. These patients should not be rechallenged with nimesulide. Liver damage, in most cases reversible, has been reported following short exposure to the drug.

Concomitant administration with known hepatotoxic drugs, and alcohol abuse must be avoided during treatment with <Nimesulide-containing medicinal products>, since they either increase the risk of hepatic reactions.

During therapy with <Nimesulide-containing medicinal products>, patients should be advised to refrain from other analgesics. Simultaneous use of different NSAIDs is not recommended.

Gastrointestinal bleeding or ulceration / perforation can occur at any time during treatment with or without warning symptoms or a previous history of gastrointestinal events. If gastrointestinal bleeding or ulceration occurs, nimesulide should be discontinued. Nimesulide should be used with caution in patients with gastrointestinal disorders, including history of peptic ulceration, history of gastrointestinal haemorrhage, ulcerative colitis or Crohn's disease.

In patients with renal or cardiac impairment, caution is required since the use of <Nimesulide-containing medicinal products> may result in deterioration of renal function. In the event of deterioration, the treatment should be discontinued (see also section 4.5).

Elderly patients are particularly susceptible to the adverse effects of NSAIDs, including gastrointestinal haemorrhage and perforation, impaired renal, cardiac and hepatic function. Therefore, appropriate clinical monitoring is advisable.

As nimesulide can interfere with platelet function, it should be used with caution in patients with bleeding diathesis (see also section 4.3). However, <Nimesulide-containing medicinal products> is not a substitute for acetylsalicylic acid for cardiovascular prophylaxis.

NSAIDs may mask the fever related to an underlying bacterial infection.

The use of <Nimesulide-containing medicinal products> may impair female fertility and is not recommended in women attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of <Nimesulide-containing medicinal products> should be considered (see section 4.6).

4.5 Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions
Patients receiving warfarin or similar anticoagulant agents or acetylsalicylic acid have an increased risk of bleeding complications, when treated with <Nimesulide-containing medicinal products>. Therefore this combination is not recommended (see also section 4.4.) and is contraindicated in

patients with severe coagulation disorders (see also section 4.3). If the combination cannot be avoided, anticoagulant activity should be monitored closely.

Pharmacodynamic/pharmacokinetic interactions with diuretics
In healthy subjects, nimesulide transiently decreases the effect of furosemide on sodium excretion and, to a lesser extent, on potassium excretion and reduces the diuretic response.
Co-administration of nimesulide and furosemide results in a decrease (of about 20%) of the AUC and cumulative excretion of furosemide, without affecting its renal clearance.
The concomitant use of furosemide and <Nimesulide containing medicinal products> requires caution in susceptible renal or cardiac patients, as described under section 4.4.

Pharmacokinetic interactions with other drugs:
Non-steroidal anti-inflammatory drugs have been reported to reduce the clearance of lithium, resulting in elevated plasma levels and lithium toxicity. If <Nimesulide containing medicinal products> are prescribed for a patient receiving lithium therapy, lithium levels should be monitored closely.

Potential pharmacokinetic interactions with glibenclamide, theophylline, warfarin, digoxin, cimetidine and an antacid preparation (i.e. a combination of aluminium and magnesium hydroxide) were also studied in vivo. No clinically significant interactions were observed.

Nimesulide inhibits CYP2C9. The plasma concentrations of drugs that are substrates of this enzyme may be increased when <Nimesulide containing medicinal products> are used concomitantly.

Caution is required if nimesulide is used less than 24 hours before or after treatment with methotrexate because the serum level of methotrexate might increase and therefore, the toxicity of this drug might increase.
Due to their effect on renal prostaglandines, prostaglandin synthetase inhibitors like nimesulide may increase the nephrotoxicity of cyclosporines.

Effects of other drugs on nimesulide:
In vitro studies have shown displacement of nimesulide from binding sites by tolbutamide, salicylic acid and valproic acid. However, despite a possible effect on plasma levels, these interactions have not demonstrated clinical significance.

4.6 Pregnancy and lactation

The use of <Nimesulide containing medicinal products> is contraindicated in the third trimester of pregnancy (see section 4.3).
Like other NSAIDs, <Nimesulide containing medicinal products> is not recommended in women attempting to conceive (see section 4.4).
As with other NSAIDs known to inhibit prostaglandin synthesis, nimesulide may cause premature closure of the ductus arteriosus, pulmonary hypertension, oliguria, oligoamnios, increased risk of bleeding, uterine inertia and peripheral oedema. There have been isolated reports of renal failure in neonates born to women taking nimesulide in late pregnancy.

Studies in rabbits have shown an atypical reproductive toxicity (see section 5.3) and no adequate data from the use of nimesulide-containing medicinal products in pregnant women are available. Therefore, the potential risk for humans is unknown and prescribing the drug during the first two trimesters of pregnancy is not recommended.

Lactation:
It is not known whether nimesulide is excreted in human milk. <Nimesulide containing medicinal products> are contraindicated when breastfeeding (see sections 4.3 and 5.3).

4.7 Effects on ability to drive and use machines

No studies on the effect of <Nimesulide containing medicinal products> on the ability to drive or use machines have been performed. However, patients who experience dizziness, vertigo or somnolence after receiving <Nimesulide containing medicinal products> should refrain from driving or operating machines.

4.8 Undesirable effects

The following listing of undesirable effects is based on data from controlled clinical trials* (approximately 7,800 patients) and from post marketing surveillance with reporting rates classified as: very common (>1/10); common (>1/100, <1/10), uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000), including isolated cases.

Blood disorders	Rare	Anaemia* Eosinophilia*
	Very rare	Thrombocytopenia Pancytopenia Purpura
Immune system disorders	Rare	Hypersensitivity*
	Very rare	Anaphylaxis
Metabolism and nutrition disorders	Rare	Hyperkalaemia*
Psychiatric disorders	Rare	Anxiety* Nervousness* Nightmare*
Nervous system disorders	Uncommon	Dizziness*
	Very rare	Headache Somnolence Encephalopathy (Reye's syndrome)
Eye disorders	Rare	Vision blurred*
	Very rare	Visual disturbance
Ear and labyrinth disorders	Very rare	Vertigo
Cardiac disorders	Rare	Tachycardia*
Vascular disorders	Uncommon	Hypertension*
	Rare	Haemorrhage* Blood pressure fluctuation* Hot flushes*
Respiratory disorders	Uncommon	Dyspnoea*
	Very rare	Asthma Bronchospasm
Gastrointestinal disorders	Common	Diarrhoea* Nausea* Vomiting*
	Uncommon	Constipation* Flatulence* Gastritis*
	Very rare	Abdominal pain Dyspepsia Stomatitis Melaena Gastrointestinal bleeding Duodenal ulcer and perforation Gastric ulcer and perforation

Hepato-biliary disorders (see section 4.4."Special warnings and special precautions for use")	Very rare	Hepatitis Fulminant hepatitis (including fatal cases) Jaundice Cholestasis
Skin and subcutaneous tissue disorders	Uncommon	Pruritus* Rash* Sweating increased*
	Rare	Erythema* Dermatitis*
	Very rare	Urticaria Angioneurotic oedema Face oedema Erythema multiforme Stevens Johnson syndrome Toxic epidermal necrolysis
Renal and urinary disorders	Rare	Dysuria* Haematuria* Urinary retention*
	Very rare	Renal failure Oliguria Interstitial nephritis
General disorders	Uncommon	Oedema*
	Rare	Malaise* Asthenia*
	Very rare	Hypothermia
Investigations	Common	Hepatic enzymes increased*
*frequency based on clinical trial		

4.9 Overdose

Symptoms following acute NSAID overdoses are usually limited to lethargy, drowsiness, nausea, vomiting and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Hypertension, acute renal failure, respiratory depression and coma may occur, but are rare. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAIDs, and may occur following an overdose.

Patients should be managed by symptomatic and supportive care following an NSAID overdose. There are no specific antidotes. No information is available regarding the removal of nimesulide by haemodialysis, but based on its high degree of plasma protein binding (up to 97.5%) dialysis is unlikely to be useful in overdose. Emesis and/or activated charcoal (60 to 100 g in adults) and/or osmotic cathartic may be indicated in patients seen within 4 hours of ingestion with symptoms or following a large overdose. Forced diuresis, alkalinization of urine, haemodialysis, or haemoperfusion may not be useful due to high protein binding. Renal and hepatic function should be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group:
ATC code: M01AX17

Nimesulide is a non-steroidal anti-inflammatory drug with analgesic and antipyretic properties which acts as an inhibitor of prostaglandin synthesis enzyme cyclo-oxygenase.

5.2 Pharmacokinetic properties

After a single administration of <Nimesulide containing medicinal products> 200 mg suppository, a peak plasma level of about 2 mg/l is reached in 4 hours, with mean AUC of 27 mg h/l. The corresponding values at the steady state were Cmax about 3 mg/l; Tmax = 4 hours and AUC of 25 mg h/l. Moreover, <Nimesulide containing medicinal products> 200 mg suppositories were found bioequivalent to <Nimesulide containing medicinal products> 100 mg tablets, despite a longer Tmax and a reduced Cmax.

Up to 97.5% binds to plasma proteins.

Nimesulide is extensively metabolised in the liver following multiple pathways, including cytochrome P450 (CYP) 2C9 isoenzymes. Therefore, there is the potential for a drug interaction with concomitant administration of drugs which are metabolised by CYP2C9 (see under section 4.5). The main metabolite is the para-hydroxy derivative which is also pharmacologically active. The lag time before the appearance of this metabolite in the circulation is short (about 0.8 hour) but its formation constant is not high and is considerably lower than the absorption constant of nimesulide. Hydroxynimesulide is the only metabolite found in plasma and it is almost completely conjugated. $T_{½}$ is between 3.2 and 6 hours.

Nimesulide is excreted mainly in the urine (approximately 50% of the administered dose).
Only 1-3% is excreted as the unmodified compound. Hydroxynimesulide, the main metabolite is found only as a glucuronate. Approximately 29% of the dose is excreted after metabolism in the faeces.
The kinetic profile of nimesulide was unchanged in the elderly after acute and repeated doses.

In an acute experimental study carried out in patients with mild to moderate renal impairment (creatinine clearance 30-80 ml/min) versus healthy volunteers, peak plasma levels of nimesulide and its main metabolite were not higher than in healthy volunteers. AUC and t1/2 beta were 50% higher, but were always within the range of kinetic values observed with nimesulide in healthy volunteers. Repeated administration did not cause accumulation.
Nimesulide is contra-indicated in patients with hepatic impairment (see section 4.3).

5.3 Preclinical safety data

Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.
In repeated dose toxicity studies, nimesulide showed gastrointestinal, renal and hepatic toxicity.
In reproductive toxicity studies, embryotoxic and teratogenic effects (skeletal malformations, dilatation of cerebral ventricles) were observed in rabbits, but not in rats, at maternally non-toxic dose levels. In rats, increased mortality of offspring was observed in the early postnatal period and nimesulide showed adverse effects on fertility.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

6.2 Incompatibilities

6.3 Shelf life

6.4 Special precautions for storage

6.5 Nature and contents of the container

6.6 Instructions for use/handling

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTORISATION NUMBER

9. DATE OF FIRST AUTHORISATION /RENEWAL OF AUTHORISATION

10. DATE OF (PARTIAL) REVISION OF THE TEXT

SUMMARY OF PRODUCT CHARACTERISTICS

NIMESULIDE 3% GEL / CREAM

1. NAME OF THE MEDICINAL PRODUCT

<TRADENAME>

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Nimesulide 3% gel / cream contains 3% w/w nimesulide (1 g of gel / cream contains 30 mg of nimesulide)
For excipients, see section 6.1

3. PHARMACEUTICAL FORM

Gel : <Company-specific>
Cream : <Company-specific>

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Symptomatic relief of pain associated with sprains and acute traumatic tendinitis.

4.2 Posology and method of administration

Adults**:** Nimesulide 3% gel / cream (usually 3 g, corresponding to a line 6-7 cm long) should be applied in a thin layer to the affected area 2-3 times daily and massaged until it is completely absorbed.
Duration of treatment: 7 – 15 days.
Children under 12 years**:** Nimesulide 3% gel / cream has not been studied in children. Therefore, safety and efficacy have not been established and the product should not be used in children (see section 4.3)**.**

4.3 Contraindications

Known hypersensitivity to nimesulide or to any other excipients in the gel / cream.
Use in patients in whom aspirin, or other medicinal products inhibiting prostaglandin synthesis, induced allergic reactions such as rhinitis, urticaria or bronchospasm.
Use on broken or denuded skin or in the presence of local infection.
Simultaneous use with other topical creams.
Use in children under 12 years.

4.4 Special warnings and special precautions for use

Nimesulide 3% gel / cream should not be applied to skin wounds or open injuries.
Nimesulide 3% gel / cream should not be allowed to come into contact with the eyes or mucous membranes; in case of accidental contact, wash immediately with water.
The product should never be taken by mouth. Hands should be washed after applying the product.
Nimesulide 3% gel / cream should not be used with occlusive dressings.
Nimesulide 3% gel / cream is not recommended for use in children under 12 years (see section 4.3) .
Undesirable effects may be reduced by using the minimum effective dose for the shortest possible duration.

Patients with gastro-intestinal bleeding, active or suspected peptic ulcer, severe renal or hepatic dysfunction, severe coagulation disorders or severe/non controlled heart failure should be treated with caution.

Since nimesulide gel 3% / cream has not been studied in hypersensitive subjects, particular caution should be used when treating patients with known hypersensitivity to other NSAIDs. The possibility of developing hypersensitivity in the course of therapy cannot be excluded.
Since with other topical NSAIDs burning sensation and exceptionally photodermatitis can occur, care should be taken during treatment with Nimesulide 3% gel / cream.
To reduce the risk of photosensitivity, patients should be warned against exposure to direct and solarium sunlight.

If symptoms persist or the condition is aggravated medical advice should be sought.

4.5 Interaction with other medicinal products and other forms of interaction

No interactions of Nimesulide 3% gel / cream with other medicinal products are known or to be expected via the topical route.

4.6 Pregnancy and lactation

There are no data relevant to the topical use of <nimesulide containing medicinal product> in pregnant women or during breastfeeding. Therefore, nimesulide 3% gel / cream should not be used during pregnancy or lactation unless clearly necessary.

4.7 Effects on ability to drive and use machines

No studies on the effect of nimesulide 3% gel / cream on the ability to drive and use machines have been performed.

4.8 Undesirable effects

The following side effects listing is based on reports from clinical studies, in a limited numbers of patients, where mild local reactions have been reported. The reporting rates are classified as: very common (>1/10); common (>1/100, <1/10), uncommon (>1/1,000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000), including isolated cases.

Skin and subcutaneous tissue disorders (see also section 4.4)	Common	Itching Erythema

4.9 Overdose

Intoxication with nimesulide as a result of topical application of Nimesulide 3% gel or cream is not to be expected since the highest plasma levels of nimesulide following application of Nimesulide 3% gel / cream are far below those found following systemic administration**.**

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: ATC code: M02AA.
Non-steroidal anti-inflammatory drug (NSAID) for topical use.
Nimesulide is an inhibitor of the prostaglandin synthesis enzyme cyclo-oxygenase.

Cyclo-oxygenase produces prostaglandins, some of them being implicated in the development and maintenance of inflammation.

5.2 Pharmacokinetic properties

When Nimesulide 3% is applied topically, plasma concentrations of nimesulide are very low in comparison with those achieved following oral intake. After a single application of 200mg of nimesulide, in the gel form, the highest plasma level of 9.77 ng/ml was noted after 24 hours. No trace of the main metabolite 4-hydroxy-nimesulide, was detected. At steady-state (day 8) peak plasma concentrations were higher (37.25 ± 13.25 ng/ml, but almost 100 times lower than those measured following repeated oral administration.

5.3 Preclinical safety data

The local tolerance and the irritation and sensitisation potential of Nimesulide 3% have been tested in several recognised animal models. The results of these studies indicate that Nimesulide 3% is well tolerated.

Preclinical data for systemically administered nimesulide reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential. In repeated dose toxicity studies, nimesulide showed gastrointestinal, renal and hepatic toxicity. In reproductive toxicity studies, embryotoxic and teratogenic effects (skeletal malformations, dilatation of cerebral ventricles) were observed in rabbits, but not in rats, at maternally non-toxic dose levels. In rats, increased mortality of offspring was observed in the early postnatal period and nimesulide showed adverse effects on fertility.

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ANNEX IV
CONDITIONS OF THE MARKETING AUTHORISATIONS

Conditions of the Marketing Authorisations

CPMP requirements in relation to post-marketing data and communication

Post-marketing data

6-monthly Periodic Safety Update Report should be provided to the National Authorities. Such report should include a specific overview on hepatic reactions and on the relationship between hepatic reactions and potential risk factors such as age >65, gender, co-administration of other medicinal products. In each of the PSURs, all hepatic ADRs should be reviewed in detail.

Communication

The MAHs should inform the public of the finalisation of the referral and of the revised conditions of nimesulide use. This information should be done via a Dear Doctor Letter (DDL), to be agreed in due time with the National Authorities so its distribution coincides with the Commission Decision on this issue.