

**ANNEX I**

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

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Austria	CSC Pharmaceuticals Handels GmbH, Heiligenstädter Str. 395 b, A-1190 Vienna	Aulin 100 mg - Tabletten	100 mg	Tablet	oral use
Austria	CSC Pharmaceuticals Handels GmbH, Heiligenstädter Str. 395 b, A-1190 Vienna	Aulin 100 mg - Granulat	100 mg	Granules for oral suspension	oral use
Austria	CSC Pharmaceuticals Handels GmbH, Heiligenstädter Str. 395 b, A-1190 Vienna	Aulin 100 mg - Suppositorien	100 mg	Suppository	rectal use
Austria	CSC Pharmaceuticals Handels GmbH, Heiligenstädter Str. 395 b, A-1190 Vienna	Aulin 200 mg - Suppositorien	200 mg	Suppository	rectal use
Austria	CSC Pharmaceuticals Handels GmbH, Heiligenstädter Str. 395 b, A-1190 Vienna	Mesulid 100 mg - Tabletten	100 mg	Tablet	oral use
Austria	CSC Pharmaceuticals Handels GmbH, Heiligenstädter Str. 395 b, A-1190 Vienna	Mesulid 100 mg - Granulat	100 mg	Granules for oral suspension	oral use
Austria	CSC Pharmaceuticals Handels GmbH, Heiligenstädter Str. 395 b, A-1190 Vienna	Mesulid 100 mg - Suppositirien	100 mg	Suppository	rectal use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Austria	CSC Pharmaceuticals Handels GmbH, Heiligenstädter Str. 395 b, A-1190 Vienna	Mesulid 200 mg - Suppositorien	200 mg	Suppository	rectal use
Belgium	THERABEL PHARMA S.A., Rue E.Van Ophem, 108 B-1180 Uccle	AULIN 100 MG	100 mg	Tablet	oral use
Belgium	THERABEL PHARMA S.A., Rue E.Van Ophem, 108 B-1180 Uccle	AULIN 100 MG	100 mg	Granules for oral suspension	oral use
Belgium	THERABEL PHARMA S.A., Rue E.Van Ophem, 108 B-1180 Uccle	MESULID	100 mg	Granules for oral suspension	oral use
Belgium	THERABEL PHARMA S.A., Rue E.Van Ophem, 108 B-1180 Uccle	MESULID 100 MG	100 mg	Tablet	oral use
Bulgaria	Tchaika Pharma Sofia 1172 1, G. M. Dimitrov Blvd.	AllGone	100 mg	Effervescent tablet	oral use
Bulgaria	Sopharma Sofia 1220 16, Iliensko shosse	Ameolin	100 mg	Tablet	oral use
Bulgaria	CSC Pharmaceuticals Sofia 1592 10, Assen Jordanov street		100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Bulgaria	CSC Pharmaceuticals Sofia 1592 10, Assen Jordanov street	Aulin 100	100 mg	Granules	oral use
Bulgaria	Inbioteh Sofia 1000 5, Triaditza street "Sofia palace"	Biolin	100 mg	Tablet	oral use
Bulgaria	ZentivaSofia 1407 25, N.Vaptzarov Blvd.	Coxtral	100 mg	Tablet	oral use
Bulgaria	Actavis Sofia 1000 2, Kniaginia Maria Luisa Blvd.	Enetra	100 mg	Tablet	oral use
Bulgaria	Medochemie Sofia 1113 20, Fr. Jolio Currie street	Aponil	100 mg	Tablet	oral use
Bulgaria	CSC Pharmaceuticals Sofia 1592 10, Assen Jordanov street	Nimed	100 mg	Tablet	oral use
Bulgaria	Laboratori Guidotti S.p.A.(Menarini Group) Sofia 1113 17, Kosta Lultchev street	Nimesil	100mg	Granules	oral use
CZ - Czech Republic	MEDICOM INTERNATIONAL S.R.O., Pátevní 7 635 00 Brno, Czech Republic	AULIN	100 mg	Granules for oral solution	Oral use
CZ - Czech Republic	MEDICOM INTERNATIONAL S.R.O., Pátevní 7 635 00 Brno, Czech Republic	AULIN	100 mg	Tablet	Oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
CZ - Czech Republic	ZENTIVA, a.s. Empiria Palace Na strži 63 140 62 Praha 4, Czech Republic	COXTRAL 100 MG TABLETY	100 mg	Tablet	Oral use
CZ - Czech Republic	CSC Pharmaceuticals Handels GmbH Gewerbestrasse 18-20 A-2102 Bisamberg, Austria	MESULID	100 mg	Granules for oral solution	Oral use
CZ - Czech Republic	MEDICOM INTERNATIONAL S.R.O., Pátevní 7 635 00 Brno, Czech Republic	NIMED	100 mg	Tablet	Oral use
CZ - Czech Republic	LABORATORI GUIDOTTI S.p.A., Via Livornese 897, I - 56010 La Vettola, PISA, Italy	NIMESIL	100 mg	Granules for oral suspension	Oral use
Cyprus	MEDOCHEMIE LTD, POBOX 51409, 3505 LEMESOS, CYPRUS	APONIL	100 mg	Tablet	ORAL
Cyprus	CDL PHARMACEUTICAL LTD, POBOX 40981, 6308 LARNACA, CYPRUS	ELINAP	100 mg	Tablet	ORAL
Cyprus	CHR. K. UNIMED LTD, 21 DAVLOU, PLATI, 2114 AGLANTZIA, LEFKOSIA, CYPRUS	FLOGOSTOP	100 mg	Tablet	ORAL

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Cyprus	P T HADJIGEORGIU CO LTD, POBOX 53158, 3301 LEMESOS, CYPRUS	NIMELIDE	100 mg	Tablet	ORAL
Cyprus	CODAL SYNTO LTD, POBOX 51785, 3508 LEMESOS, CYPRUS	NIMM	100 mg	Tablet	ORAL
Cyprus	THE STAR MEDICINES IMPORTERS & CO LTD, POBOX 50151, 3601 LEMESOS, CYPRUS	RITAMINE	100 mg	Tablet	ORAL
Cyprus	COSMED HOLDINGS LTD, P.O.BOX 42145, 6531 LARNACA, CYPRUS	SPECILID	100 mg	Tablet	ORAL
Estonia	Zentiva a.s. U Kabelovny 130 Dolni Mecholupy 102 37 Praha 10	COXTRAL	100 mg	Tablet	oral use
France	THERABEL LUCIEN PHARMA 123 rue Jules Guesde 92309 LEVALLOIS- PERRET Cedex France	NEXEN	100 mg	Tablet	Oral
France	THERABEL LUCIEN PHARMA 123 rue Jules Guesde 92309 LEVALLOIS- PERRET Cedex France	NEXEN	100 mg	Granules for oral solution	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
France	HELSINN BIREX PHARMACEUTICALS Ltd Damastown Mulhuddart DUBLIN 15 IRELAND	OXETIAN	100 mg	Tablet	Oral
France	HELSINN BIREX PHARMACEUTICALS Ltd Damastown Mulhuddart DUBLIN 15 IRELAND	OXETIAN	100 mg	Granules for oral solution	Oral
Greece	BOEHRINGER INGELHEIM HELLAS S.A. 5TH Km PAEANIAS- MARKOPOULO AVENUE KOROPI, ATTIKIS, 19400	MESULID	100 mg	Tablet	ORAL
Greece	BOEHRINGER INGELHEIM HELLAS S.A. 5TH Km PAEANIAS- MARKOPOULO AVENUE KOROPI, ATTIKIS, 19400	MESULID	200 mg	Suppository	RECTAL

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	BOEHRINGER INGELHEIM HELLAS S.A. 5TH Km PAEANIAS- MARKOPOULO AVENUE KOROPI, ATTIKIS, 19400	MESULID	100 mg	Granules for oral solution	ORAL
Greece	FARMEDIA A.E. ATHINAS 22 & APOLLONOS GERAKAS, ATTIKIS, 15344	MULTIFORMIL	100 mg	Tablet	ORAL
Greece	PHARMATHEN INTERNATIONAL S.A. GREECE, DERVENAKIWN 4, PALLINI, ATTIKIS 15351	BIOXIDOL	100 mg	Tablet	ORAL
Greece	ALET PHARMACEUTICALS M. ALEXANDER 121, AGIA VARVARA, 12351	SPECILID	100 mg	Tablet	ORAL
Greece	BIOSPRAY ABEE 18TH Km MARATHONOS AVENUE, PALLINI, 15344	FLOGOSTOP	100 mg	Tablet	ORAL
Greece	BIOMEDICA-CHEMICA A.E. G. LYRA 25, KATW KIFISSIA	NIMESULIDE / BIOMEDICA CHEMICA	100 mg	Tablet	ORAL



<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	LEOVAN, M. LEWN & SIA EE ARGONAFTHWN 22, ARGYROUPOLI, 16452	RISTOLZIT	100 mg	Tablet	ORAL
Greece	NORMA HELLAS A.E. MENANDROU 54, ATHENS, 10431	MYXINA	100 mg	Tablet	ORAL
Greece	GENEPHARM A.E. 18TH Km MARATHONOS AVENUE, PALLINI, ATTIKIS, 15351	NIMELIDE	100 mg	Tablet	ORAL
Greece	BROS EPE AVGIS & GALLINIS 15, N. KIFISSIA	DISCORID	100 mg	Tablet	ORAL
Greece	RAFARM AEBE KORINTHOU 12, N. PSYCHIKO, 15451	VENTOR	100 mg	Tablet	ORAL
Greece	RAFARM AEBE KORINTHOU 12, N. PSYCHIKO, 15451	VENTOR	100 mg	Granules for oral solution	ORAL
Greece	ARMEDICA A.E. AGIAS MARKELLIS 17, ATHENS, 11855	ALENCAS	100 mg	Tablet	ORAL
Greece	GAP A.E. AGISILAOU 46, AGIOS DIMITRIOS, 17341	G-REVM	100 mg	Tablet	ORAL
Greece	VIOFAR EPE ETHNIKIS ANTISTASEOS & TRIFYLLIAS, AHARNAI, 13671	VOLONTEN	100 mg	Tablet	ORAL

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	KLEVA EPE PARNITHOS AVENUE 189, AHARNAI, ATTIKIS, 13671	ELINAP	100 mg	Powder for oral solution	ORAL
Greece	KLEVA EPE PARNITHOS AVENUE 189, AHARNAI, ATTIKIS, 13671	ELINAP	100 mg	Tablet	ORAL
Greece	MINERVA PHARMAKEFTIKI A.E. KIFISSOU AVENUE 132, PERISTERI, 12131	MIN-A-PON	100 mg	Tablet	ORAL
Greece	ANFARM HELLAS A.E. K. PALEOLOGOU & PERIKLEOUS 27, HALANDRI, 15232	LEMESIL	100 mg	Tablet	ORAL
Greece	ELPEN A.E. PHARMACEUTICAL INDUSTRY, MARATHONOS AVENUE 95, PIKERMI, 19009	ROLAKET	100 mg	Tablet	ORAL
Greece	ELPEN A.E. PHARMACEUTICAL INDUSTRY, MARATHONOS AVENUE 95, PIKERMI, 19009	ROLAKET	200 mg	Suppository	RECTAL
Greece	ANTOR EPE P. MAVROMIHALI 1, VRILISSIA, 15235	MELIMONT	100 mg	Tablet	ORAL

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	HELP ABEE VALAORITOU 10, METAMORFOSI, ATTIKIS, 14452	MOSUOLIT	100 mg	Tablet	ORAL
Greece	FINIXFARM EPE DERVENAKION 38 & SAHINI, GERAkas, 15344	KARTAL	100 mg	Tablet	ORAL
Greece	PHARMACEUTICAL INDUSTRY PROEL EPAM. G. KORONIS DILou 9, PERISTERI, ATTIKIS, 12134	FLADALGIN	100 mg	Tablet	ORAL
Greece	REMEK PHARMACEUTICALS ABEE PENTELIS 34, PALAIO FALIRO, ATTIKIS, 17564	MESUPON	100 mg	Tablet	ORAL
Greece	FARMANIC CHEMIPHARMA S.A. FYLIS 137, KAMATERO, ATTIKIS, 13451	CHEMISULIDE	100 mg	Tablet	ORAL
Greece	REMEDINA ABEE GOUNARI 25 & AREOS, KAMATERO, ATTIKIS, 13451	AMOCETIN	100 mg	Tablet	ORAL
Greece	COSMOPHARM EPE P.O. BOX 42, KORINTHOS, 20100	LIZEPAT	100 mg	Tablet	ORAL

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	DEMO ABEE 21ST Km NATIONAL HIGHWAY ATHENS- LAMIA, 14565	RITAMINE	100 mg	Tablet	ORAL
Greece	BALU EPE 30 Km ATHENS- LAVRION, MARKOPOULO	NIBERAN	100 mg	Tablet	ORAL
Greece	SANDOZ GMBH, KUNDL, AUSTRIA BIOCHEMIESTRASSE 10, A-6250, KUNDL AUSTRIA	NIMESULIDE / HEXAL	100 mg	Tablet	ORAL
Greece	SANDOZ GMBH, KUNDL, AUSTRIA BIOCHEMIESTRASSE 10, A-6250, KUNDL AUSTRIA	NIMESULIDE / HEXAL	100 mg	Powder for oral solution	ORAL
Greece	VELKA HELLAS AEBE KAPODISTRIOU & KORINTHOU 12, NEO PSYCHIKO, 15451	NAOFID	100 mg	Tablet	ORAL
Greece	DOCTUM A.E. K.T. GIOKARIS & SIA 1 Km PAEANIAS- MARKOPOULOU AVENUE, PAEANIA, ATTIKIS, 19002	ERLECIT	100 mg	Tablet	ORAL
Greece	VOCATE PHARMAKEFTIKI A.E. GOUNARI 150, GLYFADA, 16674	TRANZICALM	100 mg	Tablet	ORAL

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	MEDICHROM A.E. 6 Km MARKOPOULOU-KOROPI AVENUE, MARKOPOULO, MESOGEION, 19003	NIMESUL	100 mg	Tablet	ORAL
Greece	FARAN ABEE PRODUCTION AND TRADING MEDICINES AVEROF 19A, ATHENS, 10433	AFLOGEN	100 mg	Tablet	ORAL
Greece	GEROLYMATOS P.N. AEBE ASKLEPIOU, KRYONERI, ATTIKIS	EDRIGYL	100 mg	Tablet	ORAL
Greece	GEROLYMATOS P.N. AEBE ASKLEPIOU, KRYONERI, ATTIKIS	EDRIGYL	100 mg	Granules for oral solution	ORAL
Greece	GEROLYMATOS P.N. AEBE ASKLEPIOU, KRYONERI, ATTIKIS	EDRIGYL	200 mg	Suppository	RECTAL
Greece	S.J.A. PHARM O.E. ARKOLEON 11, KATO PATISSIA, 10445	CLIOVYL	100 mg	Tablet	ORAL
Greece	COUP ABEE AGIAS VARVARAS 53- 55, DAFNI, ATHENS, 17235	MELICAT	100 mg	Tablet	ORAL
Greece	PHARMACYPRIA HELLAS A.E. PASTER 6, AMPELOKIPOI, 11521	LALIDE	100 mg	Tablet	ORAL

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	PHARMACYPRIA HELLAS A.E. PASTER 6, AMPELOKIPOLI, 11521	LALIDE	50 mg /5 ml	Oral suspension	ORAL
Greece	INTERMED ABEE KALYFTAKI 27, ATHENS	DOLOSTOP	100 mg	Tablet	ORAL
Greece	INTERMED ABEE KALYFTAKI 27, ATHENS	DOLOSTOP	100 mg	Effervescent tablets	ORAL
Greece	INTERMED ABEE KALYFTAKI 27, ATHENS	DOLOSTOP	100 mg	Granules for oral solution	ORAL
Greece	INTERMED ABEE KALYFTAKI 27, ATHENS	DOLOSTOP	200 mg	Suppository	RECTAL
Greece	EVAGGELOS KALOFOLIAS & SIA O.E. MENANDROU 54, ATHENS, 10431	ALGOVER	100 mg	Tablet	ORAL
Greece	FARMILIA E.E. FAVIEROU 48, ATHENS	AUROMELID	100 mg	Tablet	ORAL
Greece	AURORA PHARMACEUTICALS EPE EVROU & MESSINIAS, GERAKAS, 15344	SUDINET	100 mg	Tablet	ORAL
Greece	LEOVAN M. LEON & SIA E.E. ARGONAFTON 22, ARGYROUPOLI, 16452	LASAZIN	100 mg	Tablet	ORAL

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	PHARMACHEM EPE YMITOU 73, VRILISSIA, ATTIKIS, 15235	NIMESULIDE / PHARMACHEM	100 mg	Tablet	ORAL
Greece	ANTONIOS POLYCHRONIS OF MARINOU IONIAS 29, NEO PSYCHIKO, 15451	OMNIBUS	100 mg	Tablet	ORAL
Greece	ZWITTER PHARMACEUTICALS EPE, GREECE PENTELES AVENUE 34- 36, ATHENS, 15234	RHEMID	100 mg	Tablet	ORAL
Greece	MED-ONE S.A., HELLAS PARNITHOS AVENUE 211, AHARNAI, 13671	ALGOSULID	100 mg	Tablet	ORAL
Greece	MED-ONE S.A., HELLAS PARNITHOS AVENUE 211, AHARNAI, 13671	ALGOSULID	100 mg	Powder for oral solution	ORAL
Greece	LAMDA PHARMAKEFTIKI A.E. EVRIPIDOU 18, ATHENS, 10559	NIMESORAL	100 mg	Tablet	ORAL
Greece	MEDARTE FARMAKEFTIKI ABEE SPYROU VRETTOU 10, METAMORFOSI, 14452	NIMESULIDE / MEDICON	100 mg	Tablet	ORAL

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	FARMAMUST EPE PANTAZOPOULOU SQUARE 7, KOLONOS, ATTIKIS, 10443	LOVIREM	100 mg	Tablet	ORAL
Greece	B.I. FARMA A.E. ARISTOTELOUS 79-81, ATHENS, 10434	NIMESULIDE / B.I. FARMA	100 mg	Tablet	ORAL
Greece	LAVIPHARM HELLAS A.E. AGIAS MARINAS, PAEANIA, ATTIKIS, 19002	AULIN	100 mg	Tablet	ORAL
Greece	LAVIPHARM HELLAS A.E. AGIAS MARINAS, PAEANIA, ATTIKIS, 19002	AULIN	200 mg	Suppository	RECTAL
Greece	LAVIPHARM HELLAS A.E. AGIAS MARINAS, PAEANIA, ATTIKIS, 19002	AULIN	100 mg	Granules for oral solution	ORAL
Hungary	Chinoin Zrt.1045 Budapest, Tó u.1-5.	Winsulid	100 mg	Granules	oral
Hungary	Chinoin Zrt.1045 Budapest, Tó u.1-5.	Winsulid	100 mg	Tablet	oral
Hungary	Sanofi-Aventis 1045 Budapest, Tó u.1-5	Mesulid	100 mg	Granules	oral



<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Hungary	Sanofi-Aventis 1045 Budapest, Tó u.1-5	Mesulid	100 mg	Tablet	oral
Hungary	PannonPharma Gyógyszergyártó Kft. 1016 Budapest Derék u.2.	Nimelid	100 mg	Tablet	oral
Hungary	Eurodrug Lab.BV 4032 Debrecen,Bartha Boldizsár u.7.	Nidol	100 mg	Tablet	oral
Hungary	Lab.Guidotti S.p.A. 2040 Budaörs,Terrapark, Neumann János u.1/B tömb, D ép.	Xilox	100 mg	Granules	oral
Ireland	Helsinn Birex Pharm. Ltd. Damastown Mulhuddart Dublin 15 Ireland	Aulin	100mg	Tablet	Oral
Ireland	Helsinn Birex Pharm. Ltd. Damastown Mulhuddart Dublin 15 Ireland	Aulin	100mg	Granules	Oral
Ireland	Helsinn Birex Therapeutics Ltd. Damastown Mulhuddart Dublin 15 Ireland	Mesulid	100mg	Tablet	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Ireland	Helsinn Birex Therapeutics Ltd. Damastown Mulhuddart Dublin 15 Ireland	Mesulid	100mg	Granules	Oral
Ireland	Pinewood Laboratories Ltd Ballymacarbry Clonmel Co. Tipperary Ireland	Mesine	100mg	Tablet	Oral
Ireland	PCO Manufacturing Ltd. Unit 222 Western Industrial Estate, Naas Road, Dublin 12 Ireland	Aulin	100mg	Tablet	Oral
Ireland	B + S Healthcare Unit 4 Bradfield Road, Ruislip, Middlesex HA4, United Kingdom	Aulin	100mg	Granules	Oral
Ireland	B + S Healthcare Unit 4 Bradfield Road, Ruislip, Middlesex HA4, United Kingdom	Aulin	100mg	Tablet	Oral
Italy	FRANCIA FARMAC.IND.FAR.BIO. Srl Via DEI PESTAGALLI, 7 20138 MILANO	ALGIMESIL	100 mg	Granules	oral use
Italy	FRANCIA FARMAC.IND.FAR.BIO. Srl Via DEI PESTAGALLI, 7 20138 MILANO	ALGIMESIL	100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	SIAR PHARMA Srl, VIA VERDI 33, 20060 BUSSERO	ALGOLIDER	100 mg	Granules	oral use
Italy	SIAR PHARMA Srl, VIA VERDI 33, 20060 BUSSERO	ALGOLIDER	100 mg	Tablet	oral use
Italy	SELVI LABORAT.BIOTERAPI CO SpA, VIA PROCOIO, 28, 00065 FIANO ROMANO	ANTALGO	100 mg	Granules	oral use
Italy	ECOBI FARMACEUTICI Sas, VIA E.BAZZANO, 26, 16019 RONCO SCRIVIA	AREUMA	200 mg	Suppository	rectal use
Italy	ECOBI FARMACEUTICI Sas, VIA E.BAZZANO, 26, 16019 RONCO SCRIVIA	AREUMA	100 mg	Granules	oral use
Italy	ECOBI FARMACEUTICI Sas, VIA E.BAZZANO, 26, 16019 RONCO SCRIVIA	AREUMA	100 mg	Tablet	oral use
Italy	ROCHE SpA, P.ZZA DURANTE, 11, 20131 MILANO	AULIN	200 mg	Suppository	rectal use
Italy	ROCHE SpA, P.ZZA DURANTE, 11, 20131 MILANO	AULIN	100 mg	Granules	oral use
Italy	ROCHE SpA, P.ZZA DURANTE, 11, 20131 MILANO	AULIN	100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	ROCHE SpA, P.ZZA DURANTE, 11, 20131 MILANO	AULIN BETA	400 mg	Granules	oral use
Italy	ROCHE SpA, P.ZZA DURANTE, 11, 20131 MILANO	AULIN BETA	400 mg	Tablet	oral use
Italy	ROCHE SpA, P.ZZA DURANTE, 11, 20131 MILANO	AULIN MITE	50 mg	Granules	oral use
Italy	AGIPS FARMACEUTICI Srl, VIA AMENDOLA, 4, 16035 RAPALLO	DELFOFOS	100 mg	Granules	oral use
Italy	AGIPS FARMACEUTICI Srl, VIA AMENDOLA, 4, 16035 RAPALLO	DELFOFOS	100 mg	Tablet	oral use
Italy	SARDA PHARMACEUTICA Srl, VIA CASTIGLIONE 92/B 09100 CAGLIARI	DIMESUL	100 mg	Granules	oral use
Italy	SO.SE.PHARM Srl, VIA DEI CASTELLI ROMANI, 22, 00040 POMEZIA	DOMES	100 mg	Granules	oral use
Italy	SO.SE.PHARM Srl, VIA DEI CASTELLI ROMANI, 22, 00040 POMEZIA	DOMES	100 mg	Tablet	oral use
Italy	SO.SE.PHARM Srl, VIA DEI CASTELLI ROMANI, 22, 00040 POMEZIA	DOMES	100 mg	Orodispersible tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	SIFI SpA, VIA ERCOLE PATTI 36, 95020 LAVINAIO - ACI S.ANTONIO	EDEMAX	100 mg	Granules	oral use
Italy	SIFI SpA, VIA ERCOLE PATTI 36, 95020 LAVINAIO - ACI S.ANTONIO	EDEMAX	100 mg	Tablet	oral use
Italy	AESCVLAPIUS FARMACEUTICI Srl, VIA COZZAGLIO, 24, 25125 BRESCIA	EFRIDOL	100 mg	Granules	oral use
Italy	AESCVLAPIUS FARMACEUTICI Srl, VIA COZZAGLIO, 24, 25125 BRESCIA	EFRIDOL	100 mg	Tablet	oral use
Italy	I.B.N. SAVIO Srl, VIA E.BAZZANO, 14, 16019 RONCO SCRIVIA	EUDOLENE	100 mg	Granules	oral use
Italy	NCSN FARMACEUTICI Srl, VIA SVETONIO, 6, 00136 ROMA	FANSIDOL	100 mg	Granules	oral use
Italy	NCSN FARMACEUTICI Srl, VIA SVETONIO, 6, 00136 ROMA	FANSIDOL	100 mg	Capsule	oral use
Italy	SOFAR SpA, VIA ISONZO, 8, 20100 MILANO	FANSULIDE	100 mg	Granules	oral use
Italy	SOFAR SpA, VIA ISONZO, 8, 20100 MILANO	FANSULIDE	100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	PRODOTTI FORMENTI Srl, VIA CORREGGIO, 43, 20149 MILANO	FLAMINIDE	100 mg	Granules	oral use
Italy	PRODOTTI FORMENTI Srl, VIA CORREGGIO, 43, 20149 MILANO	FLAMINIDE	100 mg	Tablet	oral use
Italy	C.T. LAB.FARMACEUTICO Srl, VILLA SAYONARA; STR.SOLARO 75/77, 18038 SANREMO	FLOLID	100 mg	Suppository	rectal use
Italy	C.T. LAB.FARMACEUTICO Srl, VILLA SAYONARA; STR.SOLARO 75/77, 18038 SANREMO	FLOLID	100 mg	Granules	oral use
Italy	C.T. LAB.FARMACEUTICO Srl, VILLA SAYONARA; STR.SOLARO 75/77, 18038 SANREMO	FLOLID	100 mg	Tablet	oral use
Italy	ALMUS Srl, VIA CESAREA, 11/10, 16121 GENOVA	IDEALID	100 mg	Tablet	oral use
Italy	MAGIS FARMACEUTICI SpA, VIA CACCIAMALI, 34-36-38/B, 25125 BRESCIA	ISODOL	100 mg	Granules	oral use
Italy	MAGIS FARMACEUTICI SpA, VIA CACCIAMALI, 34-36-38/B, 25125 BRESCIA	ISODOL	100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	BONISCONTRO & GAZZONE Srl, VIA PAVIA,6, 20136 MILANO	LEDOREN	100 mg	Granules	oral use
Italy	BONISCONTRO & GAZZONE Srl, VIA PAVIA,6, 20136 MILANO	LEDOREN	100 mg	Tablet	oral use
Italy	ALTA CARE LAB.ITALIA Srl, VIALE DELLE MILIZIE, 134, 00192 ROMA	LIDERSOLV	100 mg	Granules	oral use
Italy	ALTA CARE LAB.ITALIA Srl, VIALE DELLE MILIZIE, 134, 00192 ROMA	LIDERSOLV	100 mg	Tablet	oral use
Italy	HELSINN BIREX PHARMAC.LTD, LARGO UMBERTO BOCCIONI, 1, 21040 ORIGGIO	MESULID	200 mg	Suppository	rectal use
Italy	HELSINN BIREX PHARMAC.LTD, LARGO UMBERTO BOCCIONI, 1, 21040 ORIGGIO	MESULID	100 mg	Granules	oral use
Italy	HELSINN BIREX PHARMAC.LTD, LARGO UMBERTO BOCCIONI, 1, 21040 ORIGGIO	MESULID	100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	HELSINN BIREX PHARMAC.LTD, LARGO UMBERTO BOCCIONI, 1, 21040 ORIGGIO	MESULID FAST	400 mg	Granules	oral use
Italy	HELSINN BIREX PHARMAC.LTD, LARGO UMBERTO BOCCIONI, 1, 21040 ORIGGIO	MESULID MITE	50 mg	Granules	oral use
Italy	NEW RESEARCH Srl, V.DELLA TENUTA DI TORRENOVA142, 00133 ROMA	NERELID	100 mg	Granules	oral use
Italy	NEW RESEARCH Srl, V.DELLA TENUTA DI TORRENOVA142, 00133 ROMA	NERELID	100 mg	Capsule	oral use
Italy	I.BIR.N Srl Ist.Biot.Nazionale, VIA VITTORIO GRASSI, 9/15, 00155 ROMA	NIDE	100 mg	Granules	oral use
Italy	I.BIR.N Srl Ist.Biot.Nazionale, VIA VITTORIO GRASSI, 9/15, 00155 ROMA	NIDE	100 mg	Capsule	oral use
Italy	MOLTENI & C. F.LLI ALITTI SpA, STR.STATALE 67, LOC.GRANATIERI, 50018 SCANDICCI	NIDEMOL	200 mg	Suppository	rectal use



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Italy	MOLTENI & C. F.LLI ALITTI SpA, STR.STATALE 67, LOC.GRANATIERI, 50018 SCANDICCI	NIDEMOL	100 mg	Granules	oral use
Italy	ITALFARMACO SpA, V.LE FULVIO TESTI, 330, 20126 MILANO	NIMEDEX	400 mg	Granules	oral use
Italy	ITALFARMACO SpA, V.LE FULVIO TESTI, 330, 20126 MILANO	NIMEDEX	400 mg	Tablet	oral use
Italy	ITALFARMACO SpA, V.LE FULVIO TESTI, 330, 20126 MILANO	NIMEDEX	400 mg	Granules	oral use
Italy	KRUGHER PHARMA Srl, VIA VOLTURNO, 10/12, 50019 SESTO FIORENTINO	NIMENOL	100 mg	Granules	oral use
Italy	KRUGHER PHARMA Srl, VIA VOLTURNO, 10/12, 50019 SESTO FIORENTINO	NIMENOL	100 mg	Granules	oral use
Italy	LAB.GUIDOTTI SpA, VIA LIVORNESE, 89, 56010 LA VETTOLA - PISA	NIMESULENE	200 mg	Suppository	rectal use
Italy	LAB.GUIDOTTI SpA, VIA LIVORNESE, 89, 56010 LA VETTOLA - PISA	NIMESULENE	100 mg	Granules	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	LAB.GUIDOTTI SpA, VIA LIVORNESE, 89, 56010 LA VETTOLA - PISA	NIMESULENE	100 mg	Tablet	oral use
Italy	ANGENERICO SpA, VIA NOCERA UMBRA, 75, 00181 ROMA	NIMESULIDE	200 mg	Suppository	rectal use
Italy	DOROM Srl, VIA GIULIO RICHARD, 7, 20143 MILANO	NIMESULIDE	200 mg	Suppository	rectal use
Italy	TEVA PHARMA ITALIA Srl, VIA GIULIO RICHARD, 7, 20143 MILANO	NIMESULIDE	200 mg	Suppository	rectal use
Italy	MERCK GENERICS ITALIA SpA, VIA AQUILEIA, 35, CINISELLO BALSAMO	NIMESULIDE	200 mg	Suppository	rectal use
Italy	DOC GENERICI Srl, VIA MANUZIO, 7, 20124 MILANO	NIMESULIDE	200 mg	Suppository	rectal use
Italy	EG SpA, VIA DOMENICO SCARLATTI, 31, 20124 MILANO	NIMESULIDE	100 mg	Chewable tablet	oral use
Italy	BENEDETTI SpA, VICOLO DE'BACCHETTONI, 1, 51100 PISTOIA	NIMESULIDE	100 mg	Granules	oral use
Italy	BENEDETTI SpA, VICOLO DE'BACCHETTONI, 1, 51100 PISTOIA	NIMESULIDE	100 mg	Granules	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	MIPHARM SpA, VIA QUARANTA, 12, 20141 MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	FARMAC.FORMENTI SpA, VIA CORREGGIO, 43, 20149 MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	SANDOZ SpA, L.GO U.BOCCIONI, 1, 21040 ORIGGIO	NIMESULIDE	100 mg	Granules	oral use
Italy	LABORATORI ALTER Srl, VIA EGADI, 7, 20144 MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	ANGENERICO SpA, VIA NOCERA UMBRA, 75, 00181 ROMA	NIMESULIDE	100 mg	Granules	oral use
Italy	DOROM Srl, VIA GIULIO RICHARD, 7, 20143 MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	POLIFARMA SpA, VIALE DELL'ARTE, 69, 00144 ROMA	NIMESULIDE	100 mg	Granules	oral use
Italy	TEVA PHARMA ITALIA Srl, VIA GIULIO RICHARD, 7, 20143 MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	MERCK GENERICS ITALIA SpA, VIA AQUILEIA, 35, 20092 CINISELLO BALSAMO	NIMESULIDE	100 mg	Granules	oral use

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Italy	GET Srl, 'VIA DANTE ALIGHIERI, 73, 18038 SANREMO	NIMESULIDE	100 mg	Granules	oral use
Italy	JET GENERICI Srl, VIA MARIO LALLI, 8, 56127 PISA	NIMESULIDE	100 mg	Granules	oral use
Italy	ROBIN Srl, P.LE DURANTE FRANCESCO, 11, MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	DOC GENERICI Srl, VIA MANUZIO, 7, 20124 MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	EG SpA, VIA DOMENICO SCARLATTI, 31, 20124 MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	RATIOPHARM GMBH, VIALE MONZA, 270, 20128 MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	RANBAXY ITALIA SpA, P.ZA FILIPPO MEDA 3, 20121 MILANO	NIMESULIDE	100 mg	Granules	oral use
Italy	PLIVA PHARMA SpA, VIA TRANQUILLO CREMONA, 10, 20092 CINISELLO BALSAMO	NIMESULIDE	100 mg	Granules	oral use
Italy	ALMUS Srl, VIA CESAREA, 11/10, 16121 GENOVA	NIMESULIDE	100 mg	Granules	oral use

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Italy	HEXAL SpA, VIA PARACELSO, 16, 20041 AGRATE BRIANZA	NIMESULIDE	100 mg	Granules	oral use
Italy	UNION HEALTH Srl, VIA ROCCAMANDOLFI, 1, 00156 ROMA	NIMESULIDE	100 mg	Granules	oral use
Italy	BENEDETTI SpA, VICOLO DE'BACCHETTONI, 1, 51100 PISTOIA	NIMESULIDE	100 mg	Tablet	oral use
Italy	MIPHARM SpA, VIA QUARANTA, 12, 20141 MILANO	NIMESULIDE	100 mg	Tablet	oral use
Italy	FARMAC.FORMENTI SpA, VIA CORREGGIO, 43, 20149 MILANO	NIMESULIDE	100 mg	Tablet	oral use
Italy	LABORATORI ALTER Srl, VIA EGADI, 7, 20144 MILANO	NIMESULIDE	100 mg	Tablet	oral use
Italy	TEVA PHARMA ITALIA Srl, VIA GIULIO RICHARD, 7, 20143 MILANO	NIMESULIDE	100 mg	Tablet	oral use
Italy	MERCK GENERICS ITALIA SpA, VIA AQUILEIA, 35, 20092 CINISELLO BALSAMO	NIMESULIDE	100 mg	Tablet	oral use
Italy	GET Srl, 'VIA DANTE ALIGHIERI, 73, 18038 SANREMO	NIMESULIDE	100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	ROBIN Srl, P.LE DURANTE FRANCESCO, 11, MILANO	NIMESULIDE	100 mg	Tablet	oral use
Italy	DOC GENERICI Srl, VIA MANUZIO, 7, 20124 MILANO	NIMESULIDE	100 mg	Tablet	oral use
Italy	EG SpA, VIA DOMENICO SCARLATTI, 31, 20124 MILANO	NIMESULIDE	100 mg	Tablet	oral use
Italy	RATIOPHARM GMBH, VIALE MONZA, 270, 20128 MILANO	NIMESULIDE	100 mg	Tablet	
Italy	RANBAXY ITALIA SpA, P.ZA FILIPPO MEDA 3, 20121 MILANO	NIMESULIDE	100 mg	Tablet	oral use
Italy	PLIVA PHARMA SpA, VIA TRANQUILLO CREMONA, 10, 20092 CINISELLO BALSAMO	NIMESULIDE	100 mg	Tablet	oral use
Italy	HEXAL SpA, VIA PARACELSO, 16, 20041 AGRATE BRIANZA	NIMESULIDE	100 mg	Tablet	oral use
Italy	UNION HEALTH Srl, VIA ROCCAMANDOLFI, 1, 00156 ROMA	NIMESULIDE	100 mg	Tablet	oral use
Italy	EG SpA, VIA DOMENICO SCARLATTI, 31, 20124 MILANO	NIMESULIDE	100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	RATIOPHARM GMBH, VIALE MONZA, 270, 20128 MILANO	NIMESULIDE	100 mg	Tablet	oral use
Italy	SANDOZ SpA, L.GO U.BOCCIONI, 1, 21040 ORIGGIO	NIMESULIDE	100 mg	Capsule	oral use
Italy	FARMAC.CABER SpA, VIALE CITTA' D'EUROPA, 681, ROMA	NIMS	100 mg	Granules	oral use
Italy	LEVOFARMA Srl, VIA CONFORTI, 42, 84083 CASTEL SAN GIORGIO	NOALGOS	100 mg	Granules	oral use
Italy	LAMPUGNANI FARMACEUTICI SpA, VIA BIANCA MARIA VISCANTI, 20122 MILANO	NOXALIDE	100 mg	Granules	oral use
Italy	LAMPUGNANI FARMACEUTICI SpA, VIA BIANCA MARIA VISCANTI, 20122 MILANO	NOXALIDE	60 ml 5%	Drops	oral use
Italy	TAD PHARMA ITALIA Srl, VIA FELICE CASATI, 16, 20124 MILANO	ORONIME	100 mg	Orodispersible tablet	oral use
Italy	PANTAFARM Srl, VIA PALESTRO, 14, 00185 ROMA	PANTAMES	100 mg	Orodispersible tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	VECCHI & PIAM Sapa, VIA PADRE G.SEMERIA, 5, 16131 GENOVA	REMOV	100 mg	Granules	oral use
Italy	VECCHI & PIAM Sapa, VIA PADRE G.SEMERIA, 5, 16131 GENOVA	REMOV	100 mg	Tablet	oral use
Italy	IST.CHIM.INTERN RENDE Srl, VIA SALARIA, 1240, 00138 ROMA	RESULIN	200 mg	Suppository	rectal use
Italy	IST.CHIM.INTERN RENDE Srl, VIA SALARIA, 1240, 00138 ROMA	RESULIN	100 mg	Granules	oral use
Italy	IST.CHIM.INTERN RENDE Srl, VIA SALARIA, 1240, 00138 ROMA	RESULIN	100 mg	Tablet	oral use
Italy	NOVARTIS CONSUMER HEALTH SpA, LARGO UMBERTO BOCCIONI, 1, 21040 ORIGGIO	REUMALIDE	200 mg	Suppository	rectal use
Italy	NOVARTIS CONSUMER HEALTH SpA, LARGO UMBERTO BOCCIONI, 1, 21040 ORIGGIO	REUMALIDE	100 mg	Granules	oral use
Italy	MDM SpA, VIALE PAPINIANO, 22/B, 20100 MILANO	SOLVING	100 mg	Granules	oral use



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Italy	MDM SpA, VIALE PAPINIANO, 22/B, 20100 MILANO	SOLVING	100 mg	Tablet	oral use
Italy	FARMAC.DAMOR SpA, VIA EMILIO SCAGLIONE, 27, 80145 NAPOLI	SULIDAMOR	100 mg	Granules	oral use
Italy	FARMAC.DAMOR SpA, VIA EMILIO SCAGLIONE, 27, 80145 NAPOLI	SULIDAMOR	100 mg	Tablet	oral use
Italy	FARMAC.DAMOR SpA, VIA EMILIO SCAGLIONE, 27, 80145 NAPOLI	SULIDAMOR	100 mg	Granules	oral use
Italy	FARMAC.DAMOR SpA, VIA EMILIO SCAGLIONE, 27, 80145 NAPOLI	SULIDAMOR	100 mg	Tablet	oral use
Italy	TAD PHARMA ITALIA Srl, VIA FELICE CASATI, 16, 20124 MILANO	SULIDE	100 mg	Granules	oral use
Italy	TAD PHARMA ITALIA Srl, VIA FELICE CASATI, 16, 20124 MILANO	SULIDE	100 mg	Tablet	oral use
Italy	ERREKAPPA EUROTERRAPICI SpA, VIA C.MENOTTI, 1/A, 20129 MILANO	SULMEDIL	200 mg	Suppository	rectal use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Italy	ERREKAPPA EUROTERAPICI SpA, VIA C.MENOTTI, 1/A, 20129 MILANO	SULMEDIL	100 mg	Granules	oral use
Italy	ERREKAPPA EUROTERAPICI SpA, VIA C.MENOTTI, 1/A, 20129 MILANO	SULMEDIL	100 mg	Tablet	oral use
Latvia	Helsinn Birex Pharmaceutical Ltd., Damastown, Mulhurddart, Dublin 15, Ireland	Mesulid	100 mg	Tablet	Oral
Latvia	Laboratori Guidotti S. P. A., Via Trieste 40, I- 56126 Piza, Italy	Nimesil	100 mg	granules for oral suspension	Oral
Latvia	Medochemie Ltd., P. O. Box 51409, CY-3505 Limassol, Cyprus	Aponil	100 mg	Tablet	Oral
Latvia	Zentiva a. S., Nitrianska 100, 92027 Hlohovec, Slovakia	Coxtral	100 mg	Tablet	Oral
Lithuania	Medochemie Ltd., P. O. Box 51409 CY-3505 Limassol, Cyprus	Aponil	100 mg	Tablet	oral use
Lithuania	Zentiva a. s., U kabelovny 130 102 37 Praha 10 Dolni Mecholupy, Czech Republic	Coxtral	100 mg	Tablet	oral use
Lithuania	Helsinn Birex Pharmaceuticals Ltd., Damastown Mulhuddart Dublin 15, Ireland	Mesulid	100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Lithuania	Laboratori Guidotti S.p.A., Via Livornese, 897-56010 Pisa-La Viettola, Italy	Nimesil	100 mg	granules for oral suspension	oral use
Malta	Vecchi & C Piam S A, Via Padre G Semeria, 5, Genoa 16131, Italy	Remov	100mg	Tablet	Oral
Poland	Zentiva a.s. U Kabelovny 130 Dolni Mecholupy 102 37 Prague 10	COXTRAL	100 mg	tablet	oral use
Poland	Medicom International s.r.o., Paterni 7, Brno, 63500 Czech Republik	AULIN	100 mg	Granules for oral use	oral use
Poland	LABORATORI GUIDOTTI S.p.A. Via Livornese 897 I - 56010 San Piero a Grado PISA, Italy	NIMESIL	100 mg	Tablet	oral use
Poland	Medicom International s.r.o., Paterni 7, Brno, 63500 Czech Republik	AULIN	100 mg	Granules for oral use	oral use
Portugal	Angelini Farmacêutica, Lda. Rua João Chagas, 53 - 3º 1495-764 Cruz Quebrada - Dafundo	Aulin	100 mg	Tablet	Oral
Portugal	Angelini Farmacêutica, Lda. Rua João Chagas, 53 - 3º 1495-764 Cruz Quebrada - Dafundo	Aulin	100 mg	Powder for oral suspension	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Angelini Farmacêutica, Lda. Rua João Chagas, 53 - 3º 1495-764 Cruz Quebrada - Dafundo	Aulin	200 mg	Suppository	Rectal
Portugal	Rega Farma - Promoção de Produtos Farmacêuticos, S.A. Rua João Chagas, 53 - 3º 1495-764 Cruz Quebrada	Donulide	100 mg	Tablet	Oral
Portugal	Rega Farma - Promoção de Produtos Farmacêuticos, S.A. Rua João Chagas, 53 - 3º 1495-764 Cruz Quebrada	Donulide	100 mg	Powder for oral suspension	Oral
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros	Nimalge	200 mg	Suppository	Rectal
Portugal	Vida - Produtos Farmacêuticos, S.A. Vala do Carregado 2600-726 Castanheira do Ribatejo	Nimartin	100 mg	Coated tablet	Oral
Portugal	Sanofi-Aventis - Produtos Farmacêuticos, S.A. Empreendimento Lagoas Park - Edifício 7 - 3º 2740-244 Porto Salvo	Nimed	100 mg	Coated tablet	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Sanofi-Aventis - Produtos Farmacêuticos, S.A. Empreendimento Lagoas Park - Edifício 7 - 3º 2740-244 Porto Salvo	Nimed	100 mg	Powder for oral solution	Oral
Portugal	Sanofi-Aventis - Produtos Farmacêuticos, S.A. Empreendimento Lagoas Park - Edifício 7 - 3º 2740-244 Porto Salvo	Nimed	200 mg	Suppository	Rectal
Portugal	Laboratori Guidotti, S.p.A. Via Trieste, 40 I-56126 Pisa	Nimesulene	100 mg	Powder for oral suspension	Oral
Portugal	Alter, S.A. Estrada Marco do Grilo - Zemouto 2830 Coima	Nimesulida Alter 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Arrowblue Produtos Farmacêuticos S.A. Av. D. João II, 10 Esqº - Torre Fernão de Magalhães 1998-025 Lisboa	Nimesulida Arrowblue	100 mg	Tablet	Oral
Portugal	Farmoquímica Baldacci, S.A. Rua Duarte Galvão, 44 1549-005 Lisboa	Nimesulida Baldacci 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Bluepharma - Indústria Farmacêutica, S.A. São Martinho do Bispo 3045-016 Coimbra	Nimesulida Bluepharma 100 mg Comprimidos	100 mg	Tablet	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Cicum Farma Unipessoal, Lda. Rua Alfredo da Silva, 16 2610-016 Amadora	Nimesulida Cicum 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Edol Themaxis - Produtos Farmacêuticos S.A. Avenida 25 de Abril, nº 6 - 6A 2795-195 Linda-a-Velha	Nimesulida Edol	100 mg	Tablet	Oral
Portugal	Farmoz - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros - Edifício Sagres - 3º A 2685-338 Prior Velho	Nimesulida Farmoz 100 mg Comprimidos	100 mg	Coated tablet	Oral
Portugal	Generis Farmacêutica, S.A. Office Park da Beloura - Edifício 4 - Quinta da Beloura 2710-444 Sintra	Nimesulida Generis 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Generis Farmacêutica, S.A. Office Park da Beloura - Edifício 4 - Quinta da Beloura 2710-444 Sintra	Nimesulida Generis 100 mg Granulado para Solução Oral	100 mg	Powder for oral solution	Oral
Portugal	Companhia Portuguesa Higiene Pharma - Produtos Farmacêuticos, S.A. Rua dos Bem Lembrados, 141 - Manique 2645-471 Alcabideche	Nimesulida Gerilide 100 mg Comprimidos	100 mg	Tablet	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Companhia Portuguesa Higiene Pharma - Produtos Farmacêuticos, S.A. Rua dos Bem Lembrados, 141 - Manique 2645-471 Alcabideche	Nimesulida Gerilide 100 mg Granulado para Solução Oral	100 mg	Powder for oral solution	Oral
Portugal	Germed Farmacêutica, Lda. Rua Alto do Montijo, 13 - 1º Dto - Edifício Monsanto 2790-012 Portela de Carnaxide	Nimesulida Germed 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Germed Farmacêutica, Lda. Rua Alto do Montijo, 13 - 1º Dto - Edifício Monsanto 2790-012 Portela de Carnaxide	Nimesulida Germed 100 mg Granulado para suspensão oral	100 mg	Powder for oral suspension	Oral
Portugal	gp - genéricos portugueses, Lda. Rua Henrique Paiva Couceiro, 29 - Venda Nova 2700-451 Amadora	Nimesulida gp 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Laboratórios Inibsa, S.A. Zona Industrial da Abrunheira - Edifício 1 - 2º I - Sintra Business Park 2710-089 Sintra	Nimesulida Inibsa 100 mg comprimidos	100 mg	Tablet	Oral
Portugal	Laboratórios Inibsa, S.A. Zona Industrial da Abrunheira - Edifício 1 - 2º I - Sintra Business Park 2710-089 Sintra	Nimesulida Inibsa 100 mg granulado para suspensão oral	100 mg	Powder for oral suspension	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Tecnimede - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros - Edifício Sagres - 3º A 2685-338 Prior Velho	Nimesulida Isartrox 100 mg Comprimidos	100 mg	Coated tablet	Oral
Portugal	Jaba Farmacêutica, S.A. Zona Industrial da Abrunheira - Edifício Jaba - Rua da Tapada Grande, 2 2710-089 Sintra	Nimesulida Jabasulide 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Jaba Farmacêutica, S.A. Zona Industrial da Abrunheira - Edifício Jaba - Rua da Tapada Grande, 2 2710-089 Sintra	Nimesulida Jabasulide 100 mg Granulado Para Solução Oral	100 mg	Powder for oral solution	Oral
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros	Nimesulida Labesfal	200 mg	Suppository	Rectal
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros	Nimesulida Labesfal 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros	Nimesulida Labesfal 100 mg Granulado para Suspensão Oral	100 mg	Powder for oral suspension	Oral
Portugal	Vetiquima - Produtos Químicos, Lda. Estrada Nacional 10, Km 140,260 2696-901 Bobadela	21 994 83 00	100 mg	Tablet	Oral



<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Vetiquima - Produtos Químicos, Lda. Estrada Nacional 10, Km 140,260 2696-901 Bobadela	21 994 83 00	100 mg	Powder for oral suspension	Oral
Portugal	Medicamed - Produtos Médicos e Farmacêuticos, S.A. Av. D. Afonso Henriques, 1462 - Edifício Olympus 4450-013 Matosinhos	Nimesulida Medicamed 100 mg Comprimidos	100 mg	Coated tablet	Oral
Portugal	Medineo - Comercialização de Produtos Farmacêuticos, Lda. Rua Teófilo Braga, 14 2775- 290 Parede	Nimesulida Medineo 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Mepha - Investigação, Desenvolvimento e Fabricação Farmacêutica, Lda. Rua Elias Garcia, 28 C - Edifício 4 - Venda Nova 2701-355 Amadora	Nimesulida Mepha 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Mepha - Investigação, Desenvolvimento e Fabricação Farmacêutica, Lda. Rua Elias Garcia, 28 C - Edifício 4 - Venda Nova 2701-355 Amadora	Nimesulida Mepha 100 mg Granulado para Suspensão Oral	100 mg	Powder for oral suspension	Oral
Portugal	Merck Genéricos - Produtos Farmacêuticos, Lda. Rua Alfredo da Silva, 3 C - 4º 1300-040 Lisboa		100 mg	Tablet	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Merck Genéricos - Produtos Farmacêuticos, Lda. Rua Alfredo da Silva, 3 C - 4º 1300-040 Lisboa	Nimesulida Merck Genéricos 100 mg Granulado para solução oral	100 mg	Powder for oral solution	Oral
Portugal	Tecnimede - Sociedade Técnico-Medicinal, S.A. Rua Prof. Henrique de Barros - Edifício Sagres - 3º A 2685-338 Prior Velho	Nimesulida Neuride 100 mg Comprimidos	100 mg	Coated tablet	Oral
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros	Nimesulida Nilmide 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Labesfal - Laboratórios Almiro, S.A. 3465-051 Campo de Besteiros	Nimesulida Nilmide 100 mg Granulado Para Suspensão Oral	100 mg	Powder for oral suspension	Oral
Portugal	Pharmakern Portugal - Produtos Farmacêuticos, Sociedade Unipessoal, Lda. Av. José Gomes Ferreira, 11 - 3º, Sala 31 - Edifício Atlas II 1495-139 Miraflores - Algés	Nimesulida Pharmakern 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Ranbaxy Portugal - Comércio e Desenvol. de Produtos Farmacêuticos, Unip., Lda. Rua do Campo Alegre, 1306, 3º - Sala 301/302 - Edifício Botânico 4150-174 Porto	Nimesulida Ranbaxy	100 mg	Tablet	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Ranbaxy Portugal - Comércio e Desenvol. de Produtos Farmacêuticos, Unip., Lda. Rua do Campo Alegre, 1306, 3º - Sala 301/302 - Edifício Botânico 4150-174 Porto	Nimesulida Ranbaxy	100 mg	Powder for oral suspension	Oral
Portugal	Ratiopharm - Comércio e Indústria de Produtos Farmacêuticos, Lda. Rua Quinta do Pinheiro - Edifício Tejo - 6º Piso 2790-143 Carnaxide	Nimesulida Ratiopharm 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Quiraus - Comércio Produtos Químicos e Tecnologia Farmacêutica, Lda. Av. Salvador Allende, 12 - 1º 2780-163 Oeiras	Nimesulida Reumesul 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Sandoz Farmacêutica, Lda. Rua do Centro Empresarial - Edifício 3 - Loja 1 - Quinta da Beloura 2710-693 Sintra	Nimesulida Sandoz 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Decafarma - Comércio de Produtos Farmacêuticos, Lda Centro Empresarial Sintra Estoril, V, Armazém E 3 2710-144 Sintra	Nimesulida Sulimed 100 mg Comprimidos	100 mg	Tablet	Oral
Portugal	Laboratórios Atral, S.A Vala do Carregado 2600-726 Castanheira do Ribatejo	Ribantil	100 mg	Coated tablet	Oral

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Pharmout - Farmacêutica Internacional, Lda. Rua da Quinta das Romeiras, 104 - 7º 1495-236 Algés	Vitolide	100 mg	Tablet	Oral
Romania	Faran Laboratories SA/Imedica SA, Sos. Bucuresti – Ploiesti Nr. 141D Sector 1, Bucuresti	AFLOGEN	100 mg	Tablet	oral use
Romania	Medochemie LTD, Str. Prof. Dr. Ion Cantacuzino nr. 5, sector 1, Bucuresti	Aponil	100 mg	Tablet	oral use
Romania	C.S.C. PHARMACEUTICALS, Drumul Sarii nr. 108, sector 6 Bucuresti	Aulin	100 mg	granules for oral suspension	oral use
Romania	C.S.C. PHARMACEUTICALS, Drumul Sarii nr. 108, sector 6 Bucuresti	Aulin	100 mg	Tablet	oral use
Romania	Zentiva AS, B-dul Theodor Pallady nr. 50, 032266 Bucuresti	Coxtral	100 mg	Tablet	oral use
Romania	ANFARM HELLAS SA/Imedica, Sos. Bucuresti – Ploiesti Nr. 141D Sector 1, Bucuresti	Lemesil	100 mg	Tablet	oral use
Romania	LABORATORI GUIDOTTI S.p.A., Via Livornese 897, I - 56010 La Vettola, PISA, Italy	Nimesil	100 mg	granules for oral suspension	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Romania	Terapia SA, Str. Fabricii Nr.124, 3400 Cluj Napoca, Jud. Cluj	Nimesulid	100 mg	Tablet	oral use
Romania	LABORMED PHARMA SRL, Splaiul Independentei Nr. 319, Sector 6, Bucuresti	Nimesulid LPH 100 mg	100 mg	Tablet	oral use
Romania	MAGISTRA C & C, Str. Aviator Belghiru Nr. 9, 8700 Constanta, Jud. Constanta	Nimesulid 100 mg	100 mg	Tablet	oral use
Romania	ARENA GROUP SA, Str. Stefan Mihaileanu Nr.31, Sector 2, 73101 Bucuresti	Nimesulid Arena 100 mg	100 mg	Tablet	oral use
Romania	SLAVIA PHARM SRL, Str. Stirbei Voda Nr.53-55, Sector 1, Bucuresti	Nimesulid Slavia	100 mg	Tablet	oral use
Romania	FARMACEUTICI DAMUR SPA, Calea Dorobantilor Nr.113 Ap.35, Cluj, Jud. Cluj	Sulidamor	100 mg	Powder for oral suspension	powder for oral suspension
Slovak Republic	Medicom International s.r.o., Brno, Czech Republik	AULIN 100 mg granulát	100 mg	Granules for oral use	oral use
Slovak Republic	Medicom International s.r.o., Brno, Czech Republik	AULIN 100 mg tablety	100 mg	Tablet	oral use
Slovak Republic	Zentiva a.s. , Praha, Czech Republik	COXTRAL	100 mg	Tablet	oral use

<b>Member State</b>	<b>Marketing Authorisation Holder</b>	<b>Product name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Slovak Republic	CSC Pharmaceuticals Handels GmbH, Wien, Austria	MESULID	100 mg	Tablet	oral use
Slovak Republic	Medicom International s.r.o., Brno, Czech Republik	NIMED	100 mg	Tablet	oral use
Slovak Republic	Laboratori Guidotti S. P. A., Via Livornese 897, La Vettola, 56010 Pisa, Italy	Nimesil	100 mg	Granules for oral suspension	oral use
Slovenia	CSC Pharma d.o.o. JANA HUSA 1a, SI-1000 Ljubljana Slovenia	Aulin	100 mg	Tablet	oral
Slovenia	CSC Pharma d.o.o. JANA HUSA 1a, SI-1000 Ljubljana Slovenia	Aulin	100 mg	Powder for oral suspension	oral
Spain	HELSINN BIREX PHARMACEUTICALS LTD Damastown Mulhuddart, County Dublin, 15 Ireland	GUAXAN 100 mg comprimidos	100 mg	Tablet	oral use

**ANNEX II**

**SCIENTIFIC CONCLUSIONS AND GROUNDS FOR THE MAINTENANCE OF THE  
MARKETING AUTHORISATIONS AND AMENDMENTS OF THE SUMMARY OF  
PRODUCT CHARACTERISTICS AND PACKAGE LEAFLET PRESENTED BY THE EMEA**

## SCIENTIFIC CONCLUSIONS

### OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF NIMESULIDE CONTAINING MEDICINAL PRODUCTS (SYSTEMIC FORMULATIONS) (see Annex I)

Nimesulide is a non-steroidal anti-inflammatory drug (NSAID), available only on prescription and authorised in Europe since 1985.

Nimesulide-containing medicinal products are currently marketed in more than 50 countries worldwide, particularly in Europe and South America.

In Europe, nimesulide is nationally authorised in 16 Member States (Austria, Belgium, Bulgaria, Czech Republic, Cyprus, France, Greece, Hungary, Italy, Latvia, Lithuania, Malta, Portugal, Romania, Slovakia and Slovenia).

Nimesulide was the subject of an Article 31 referral to the CHMP in 2002, following national suspension of its licence in Finland, and subsequently Spain, due to concerns regarding hepatotoxicity. This referral concluded, with divergent positions submitted by Finland, Spain and Ireland, that the benefit/risk profile of nimesulide for systemic use remained positive, subject to revision of the product information, including a restriction of the maximum oral dose to 100 mg twice daily. This decision was endorsed by the European Commission in April 2004 and the product information was subsequently amended to contraindicate its use in patients with hepatic impairment, and to include warnings about the risk of hepatitis, fulminant hepatitis (including fatal cases), jaundice and cholestasis. The harmonised product information were implemented in the Member States end of 2004-beginning of 2005.

On 15<sup>th</sup> May 2007, following new safety information regarding cases of fulminant hepatic failure associated with nimesulide, the Irish Medicines Board suspended the national marketing authorisations for all systemic medicinal products containing nimesulide available in Ireland. The Irish Medicines Board informed the EMEA, other Member States and the Marketing Authorisation Holders in accordance with Article 107(2) of Directive 2001/83/EC, as amended.

During its plenary meeting in May 2007, the CHMP considered the emerging safety data from Ireland on the risk of fulminant hepatic failure associated with nimesulide, as well as data available from published literature, and concluded that hepatotoxicity data on nimesulide should be reviewed in accordance with Article 107(2) of Directive 2001/83/EC, as amended.

The CHMP reviewed the data presented, including answers provided by the Marketing Authorisations Holders (MAHs), pharmacovigilance data provided by the Member States, data provided by the EMEA and literature review. This review focused on the hepatic safety of nimesulide in light of the significant concern arising from the Irish data and within the defined scope of the Article 107.

The hepatotoxic signal seen in Ireland showed that nimesulide was associated with more cases of non-A non-B non-paracetamol-related fulminant hepatic failure requiring liver transplantation in Ireland than any other medicinal product. Some of the cases reported were however confounded by concomittant disease/hepatotoxic medication and a clear causal relationship with nimesulide could not be concluded.

The assessment of overall post-marketing spontaneous reporting data, clinical studies, and epidemiological data, show a higher frequency of severe adverse hepatic reactions with nimesulide compared with other NSAIDs. However, with the exception of the signal of serious hepatic adverse reactions raised by Ireland, the review of the overall data submitted do not modify the safety profile of nimesulide as established after the previous CHMP opinion.

The CHMP considered the gastrointestinal toxicity profile of nimesulide as compared to other NSAIDs, and the possible consequences of switching to other NSAIDs with a higher gastrointestinal risk. The assessment of these consequences were supported by a simulation of the possible impact of



nimesulide withdrawal in Italy. This simulation showed a notable reduction of hospitalisation due to liver injuries whilst hospitalisation due to gastrointestinal toxicity might increase.

Finally, according to the data submitted by the Marketing Authorisation Holder the majority of hepatic disorders (56%), occurred after two weeks of treatment, therefore a treatment period of not longer than 15 days may limit the risk of acute liver injury.

Having considered all of the available evidence, the CHMP concluded that the data did not support a suspension of all marketing authorisations in Europe.

The CHMP agreed, that the risk minimisation measures adopted at the end of the first referral have been able to contain the incidence of the most serious liver injuries. The use of nimesulide in strict accordance with the Product Information recommendations has been shown to be equally effective in reducing hepatic toxicity. The additional Product Information restrictions together with a limitation of duration of treatment and withdrawal of the pack sizes above 30 units aim at further minimising such risk, together with the conditions (see Annex IV) and the effort of national competent authorities in education and information activities on both prescribers and patients.

The review concluded that a small increase in the absolute risk for hepatotoxic reactions associated with nimesulide cannot be excluded although the overall risk benefit/balance remains positive.

Overall, the benefit-risk profile of nimesulide-containing medicinal products for systemic use remains favourable and the Marketing Authorisations for products containing nimesulide for systemic use should be maintained with the following restrictions:

- The decision to prescribe nimesulide should be based on an assessment of the individual patient's overall risks.
- The maximum duration of a treatment course with nimesulide is 15 days. Therefore pack sizes above 30 units should be withdrawn and not authorised
- New contraindications and strengthened warnings have been added to the Summary of Product characteristics and Package Leaflet in order to limit exposure of nimesulide to those patients without risk factors for hepatic reactions.

Furthermore the maintenance of the Marketing Authorisations is linked to the conditions, below:

- Submission of 6-monthly PSURs
- Implementation of a retrospective study, followed by a prospective study in transplant centres
- Update of Risk Management Plan
- Information of healthcare professional via a 'Direct Healthcare Professional Communication' letter

## **GROUNDNS FOR THE MAINTENANCE OF THE MARKETING AUTHORISATIONS AND THE AMENDMENTS OF THE SUMMARY OF PRODUCT CHARACTERISTICS AND PACKAGE LEAFLET**

Having reviewed all available data on hepatotoxicity, the CHMP concluded the following.

- Nimesulide showed a higher frequency of severe adverse hepatic reactions but the overall safety profile of nimesulide is not modified.
- The CHMP considered the gastrointestinal toxicity profile of nimesulide and the possible consequences of switching to other NSAIDs.
- The limitation of treatment with nimesulide not longer than 15 days may limit the risk of acute liver injury.

The CHMP has recommended the maintenance of the Marketing Authorisations for all medicinal products referred to in Annex I of the Opinion and to amend the relevant sections of the Summary of Product Characteristics and Package Leaflet of systemic formulations of nimesulide, as set out in Annex III of the Opinion in accordance with Article 107(2) of Directive 2001/83/EC, as amended. Conditions of the Marketing Authorisations are identified in Annex IV of this Opinion.

**ANNEX III**

**AMENDMENTS TO THE SUMMARY OF PRODUCT CHARACTERISTICS AND  
PACKAGE LEAFLET**

## AMENDMENTS TO BE INCLUDED IN THE RELEVANT SECTIONS OF THE SUMMARY OF PRODUCT CHARACTERISTICS OF NIMESULIDE CONTAINING MEDICINAL PRODUCTS (SYSTEMIC FORMULATIONS)

*Additions appear in italics and underlined deletions in ~~italics and strikethrough~~*

### 4.1 Therapeutic indications

Treatment of acute pain (*see section 4.2*).

Symptomatic treatment of painful osteoarthritis (*see section 4.2*).

Primary dysmenorrhoea.

*Nimesulide should only be prescribed as second line treatment.*

*The decision to prescribe nimesulide should be based on an assessment of the individual patient's overall risks (see sections 4.3 and 4.4).*

### 4.2 Posology and method of administration

*The minimum effective dose should be used for the shortest duration to reduce the undesirable effects.*

*The maximum duration of a treatment course with nimesulide is 15 days.*

Nimesulide 100mg Tablets/granules should be used for the shortest possible duration, as required by the clinical situation.

Adults:

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 100mg Tablets/granules is 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 100mg Tablets/granules is contraindicated in case of severe renal impairment (creatinine clearance < 30ml/min) (see sections 4.3 and 5.2).

Hepatic impairment: the use of Nimesulide 100mg Tablets/granules 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

*Concomitant exposure to other potentially hepatotoxic substances.*

*Alcoholism, drug addiction.*

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.

Patients with fever and/or flu-like symptoms.

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 100mg Tablets/granules for the shortest possible duration (see section 4.2)

Treatment should be discontinued if no benefit is seen.

Rarely Nimesulide 100mg Tablets/granules has 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 100mg Tablets/granules (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 100mg tablets/granules treatment, since either may increase the risk of hepatic reactions.~~

During therapy with Nimesulide 100mg Tablets/granules, patients should be advised to refrain from other analgesics. Simultaneous use of different NSAIDs is not recommended.

Patients receiving nimesulide who develop fever and/or flu-like symptoms should discontinue treatment

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 100mg Tablets/granules 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 100mg Tablets/granules 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 100mg Tablets/granules 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 100mg Tablets/granules should be considered (see section 4.6).

## AMENDMENTS TO BE INCLUDED IN THE RELEVANT SECTIONS OF THE PACKAGE LEAFLET OF NIMESULIDE CONTAINING MEDICINAL PRODUCTS (SYSTEMIC FORMULATIONS)

*Additions appear in italics and underlined deletions in ~~italics and strikethrough~~*

### 1. WHAT TRADEMARK IS AND WHAT IT IS USED FOR

TRADEMARK is a non-steroidal anti-inflammatory drug (“NSAID”), with pain-killing ~~and fever-lowering~~ properties. It is used for treatment of acute pain, for the treatment of symptoms of painful osteoarthritis, and for the treatment of period pains.

*Before prescribing TRADEMARK your doctor will assess the benefits this medicine may give you against your risks of developing side effects.*

### 2. BEFORE YOU TAKE TRADEMARK

**Do not use TRADEMARK if you:**

- are hypersensitive (allergic) to nimesulide or any of the other ingredients of TRADEMARK;
- have had allergic reactions (e.g. wheezing, runny or blocked nose, hives or nettle rash) after aspirin or other non-steroidal anti-inflammatory drugs;
- had a reaction to nimesulide affecting the liver in the past;
- *are taking other medicines that are known to affect the liver, e.g. paracetamol or any other pain-killers or NSAID treatment*
- *are taking drugs of addiction, or have developed a habit that makes you dependent on drugs or other substances*
- *are a regular heavy drinker (alcohol),*
- if you have liver disease or increased liver enzymes
- have a peptic ulcer (stomach or duodenal ulcer) now or had one in the past;
- have had bleeding from the stomach or bowel;
- have had bleeding into the brain (a stroke);
- have any other problem with bleeding or any problems due to your blood not clotting;
- have heart failure or a kidney disorder (poor kidney function) or any liver disorder;
- *are suffering from fever or flu (feeling generally achy, unwell, chills or shivering or have a temperature);*
- are in the last 3 months of pregnancy;
- are breastfeeding.
- 

Do not give TRADEMARK to a child aged less than 12.

### 3. HOW TO TAKE TRADEMARK

Always take TRADEMARK exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. The usual dose is 1 <unit> of 100 mg twice a day after a meal. Use TRADEMARK for as short a period of time as possible *and for not more than 15 days in any single course of treatment.*

**Take special care with TRADEMARK**

- If you have an intolerance to some sugars, you should contact your doctor before taking this medicine.

- If you are taking any of the following as they may interact with TRADEMARK:
  - medicine to thin the blood (anti-coagulants, aspirin or other salicylates)
  - water tablets (diuretics) used for heart failure or blood pressure
  - lithium which is used to treat depression and similar conditions
  - methotrexate
  - cyclosporin

make sure that your doctor or pharmacist knows that you are taking these medicines before taking TRADEMARK.

~~— Do not take other medicines that are known to affect the liver, e.g. paracetamol or any other pain killers or NSAID treatment~~

~~— Avoid excess alcohol during treatment with TRADEMARK~~

- If during nimesulide treatment you develop symptoms that suggest a liver condition, you should stop taking nimesulide and inform your doctor immediately. Symptoms suggesting a liver condition include loss of appetite, nausea, vomiting, abdominal pain, persistent tiredness or dark urine. If you have ever suffered from peptic ulcers, bleeding from the stomach or bowel, ulcerative colitis or Crohn's disease, you should tell your doctor before taking TRADEMARK.
- If during treatment with TRADEMARK, you develop fever and/or flu-like symptoms (feeling generally achy, unwell and chills or shivering) you should stop taking the product and inform your doctor.
- If you suffer from heart or kidney disease, you should tell your doctor before taking TRADEMARK; kidney function may become worse on TRADEMARK.
- If you are elderly, your doctor may want to see you at intervals to make sure that TRADEMARK is not causing stomach, kidney, heart or liver problems.
- If you are planning a pregnancy, you should inform your doctor since TRADEMARK may decrease fertility.

**ANNEX IV**  
**CONDITIONS OF THE MARKETING AUTHORISATIONS**



## Conditions of the Marketing Authorisations

The following conditions in relation to post-marketing surveillance, studies and review and communication shall be fulfilled by the Marketing Authorisation Holders of nimesulide containing medicinal products (systemic formulation).

### Post-marketing surveillance

The MAHs should strengthen the medical review, refine the monitoring of reporting rates, and improve the quality of Individual Case Safety Reports of nimesulide.

The MAHs should expedite and submit all safety reports and case series in PSURs for nimesulide, with a six monthly periodicity. These PSURs should include a specific overview of the hepatic reactions. Hepatic reactions should be given cumulatively and for the period covered by the PSUR. Particular attention should be given to indication, dosage and duration of treatment. These PSURs should be submitted to the National Competent Authorities for assessment.

### Studies and Reviews

- The MAHs should conduct a pre-clinical study on identification of reactive metabolites and protein adduct information.
- The MAHs should conduct a review of epidemiological data to review the risk of hepatic damage from nimesulide in comparison with other NSAIDs
- The MAHs should conduct a retrospective cohort study in transplant centres. This study should address the relative risk of nimesulide in respect to other NSAIDs to cause severe hepatic reactions leading to transplants. This retrospective study should lead to a follow-up prospective study in transplant centres. The protocol should be submitted to the CHMP by 3 months after the completion of the final study report of the retrospective study for review and agreement.

The final study reports of the above studies should be submitted to the National Competent Authorities for assessment.

### Communication

- The MAHs should submit a revised Risk Management Plan for nimesulide, considering the comments raised during this procedure, to the CHMP. Further updates of the Risk Management Plan should be submitted for assessment at national level.
- The MAHs should inform healthcare professionals on the outcome of this review on nimesulide via a “Direct Healthcare Professional Communication” (DHPC) to be agreed with the CHMP. The communication shall include comprehensive information on the safety risks associated with the use of nimesulide. The draft DHPC should be submitted to the CHMP within one month after adoption of the Commission Decision.
- The MAHs should perform a monitoring activity to evaluate the effectiveness of risk communication on nimesulide. A report should be provided to the National Competent authorities for assessment every 6 months as part of the PSUR (starting within one semester after adoption of the Commission Decision).
- The MAHs should perform a survey to clarify the modes of use of nimesulide in selected EU Member States to identify potential misuse. A report should be provided to the National Competent authorities for assessment within one year after adoption of the Commission Decision.

**ANNEX V**

**DETAILED EXPLANATION OF THE REASONS FOR THE ADDITIONAL CONDITIONS  
AND RESTRICTIONS TO THE CHMP OPINION**

**BACKGROUND:**

The opinion adopted by the Committee for Medicinal Products for Human Use on 20 September 2007 recommended the maintenance of the national marketing authorisations for nimesulide-containing medicinal products with the introduction of several risk minimisation measures (limitation of the maximum duration of treatment, safety warnings in the product information, additional safety studies). A significant number of members of the Committee expressed however a divergent opinion, sustaining that the benefit/risk profile of these products should be considered negative and that the marketing authorisations should rather be revoked.

The Standing Committee for Medicinal Products for Human Use discussed the matter on 20 January 2008. In the course of the meeting, it became clear that there would be neither a qualified majority in support of a draft Commission decision following the opinion of the CHMP nor a qualified majority against it.

It also appeared that a fundamental disagreement persisted among Member States competent authorities on whether risk minimisation measures were capable of addressing the risk of hepatotoxicity of the product. Moreover, the relevance of new information was discussed in the meeting. It also appeared from the discussions that certain Member States were applying at national level measures not reflected in the harmonised product information and intended to further reduce the risks associated with nimesulide. These relate in particular to restrictions to the indications (with a limitation to second line treatment) and to conditions of use and prescription practices. It was furthermore noted that alternative products also present some risks, namely of gastrointestinal bleeding.

In view of this situation, the Commission chairman decided not to submit the draft decision to a vote by the Standing Committee during the meeting but to refer the matter to the CHMP for further examination of any new reports of suspected hepatotoxicity related to nimesulide and identification and consideration of existing national measures, such as guidelines or recommendations, in relation to the use of nimesulide with a view to recommending necessary risk minimisation measures.

By letter dated 26 June 2008, the Chairman of the CHMP has informed the Commission that following the assessment of the new additional reports and consideration of other risk minimisation measures, the assessment report was updated with the new factual information and a CHMP opinion containing the same recommendations as the September opinion was put to a vote in the CHMP. The CHMP could not reach a majority for the adoption of the opinion with the same recommendations.

It follows from the above:

- Nimesulide presents a risk of hepatotoxicity, including risk of fulminant hepatic failure.
- On the other hand, the switching from nimesulide to other Non-Steroidal Anti-inflammatory drugs may lead to an increase of gastrointestinal toxicity occurrences. Therefore, an increase in gastrointestinal toxicity events may occur if nimesulide ceases to be available.
- There are divergent views within the CHMP on the assessment of whether this risk may be addressed through risk minimisation measures allowing maintenance of the products on the market or whether the risk is such that the authorisation should be revoked.
- This disagreement was also observed in the Standing Committee meeting of 20 January 2008.

Upon recommendation from the CHMP, given that an assessment of the gastrointestinal toxicity of nimesulide was outside the scope of the review procedure under Article 107, the Commission will initiate a referral under Article 31 of Directive 2001/83/EC, under which a full risk-benefit assessment will be undertaken.

**PRESENT DECISION:**

The European Commission considers it appropriate to maintain the marketing authorisation for medicinal products containing nimesulide. The majority view within the CHMP sustained such maintenance when the committee adopted its opinion of 20 September 2007 and it appears adequate to follow this majority view. This approach is strengthened by the fact that a full risk-benefit assessment

is to be conducted in the framework an Article 31 procedure, where the risks of nimesulide will be weighted vis-à-vis the gastrointestinal risks of other products.

The risk minimisation measures proposed by the CHMP shall also be introduced as it is uncontested that the maintenance of the product in the market has to be accompanied by measures aiming at lowering the possibility of adverse events.

However, in view of the severity of the adverse events, these measures should in the Commission's perspective be further intensified by (1) limiting the prescription of nimesulide to second line treatment and by (2) introducing a clear obligation upon the marketing authorisation holder to inform healthcare professionals of the safety risks associated with this product.

The restriction of the indication to second line treatment is intended to ensure that nimesulide is not used as a routine pain killer where other treatment options which present a reduced hepatotoxic risk are available. The use of nimesulide in second line treatment is already recommended in some Member States via prescription guidelines. The restriction of the indication in the summary of the product characteristics should ensure that this prescription practice is followed in all Member States where the product is authorised.

These additional measures should contribute to minimising the risks associated with the use of nimesulide whilst awaiting the results of the Article 31 referral.

The relevant sections of the Summary of Product Characteristics and Package Leaflet of systemic formulations of nimesulide and of the Conditions of the Marketing Authorisation are amended as set out in Annexes III and IV of this Decision.