

Co-ordination group for Human Use  
EMA/H/A-31/1396  
EMA/CMDh/706121/2014

## Agreement of the co-ordination group for mutual Recognition and decentralised procedures for human use, pursuant to article 107k(1) and (2) of directive 2001/83/EC,

### **Medicinal products:**

Invented names:	see Annex I
International non-proprietary name:	testosterone
Pharmaceutical forms:	see Annex I
Strengths:	see Annex I
Routes of administration:	see Annex I

### **Basis for agreement**

Pursuant to Article 31 of directive 2001/83/EC, Estonia initiated a procedure on 27 March 2014. The notification for the procedure is appended to this agreement.

The evaluation procedure started on 10 April 2014.

The steps taken for the assessment of the referred matter are detailed in the PRAC assessment report appended to this agreement.

The recommendation was adopted by the PRAC on 9 October 2014 and is appended to this agreement.

The Co-ordination Group for Mutual Recognition and Decentralised Procedures for human use (CMDh) has considered the recommendation of PRAC in accordance with Article 107k(1) and (2) of Directive 2001/83/EC.

### **Agreement**

1. The CMDh, having considered the PRAC recommendation, agreed by consensus that the marketing authorisations for testosterone containing medicinal products should be varied.

The Icelandic and the Norwegian CMDh member(s) agree(s) with the above-mentioned agreement of the CMDh.

2. The scientific conclusions and the detailed explanation of the scientific grounds for the differences from the PRAC recommendation are set out in Annex II.

3. The amendments to be introduced to the product information of testosterone containing medicinal products are set out in Annex III.

4. The conditions to the marketing authorisation(s) of testosterone containing medicinal products are set out in Annex IV.

5. The timetable for the implementation of the agreement is set out in Annex V.

To the extent that other medicinal products containing testosterone not included Annex I are currently authorised in the EU, or are subject to future authorisation procedures by the Member States, the CMDh recommends that the Member States concerned take due consideration of the scientific conclusions set out in Annex II.

This agreement is forwarded to the Member States, to Iceland and Norway and to the marketing authorisation holders for the above mentioned medicinal products, together with its annexes and appendices.

London, 19 November 2014

A handwritten signature in black ink, appearing to read 'Peter B', followed by two horizontal lines indicating a signature line.

On behalf of the CMDh

Dr Peter Bachmann, Chair

## **Annex I**

**List of the names, pharmaceutical forms, strengths of the medicinal products, routes of administration, and marketing authorisation holders in the Member States**

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Austria	Bayer Austria GmbH Herbststrasse 6-10 1160 Wien Austria	testosterone undecanoat	Nebido 1000 mg/4 ml Injektionslösung	1000 mg/4ml	solution for injection	intramuscular use
Austria	Eli Lilly GmbH Kölbgasse 8-10 1030 Wien Austria	testosterone	Axiron 30 mg/1,5 ml Lösung zur Anwendung auf der Haut	30 mg/1,5ml	gel	cutaneous use
Austria	Laboratoires Besins International SA Rue de Bourg l'Abbè 3 75003 Paris France	testosterone	Testogel 25 mg - Gel im Beutel	25 mg	gel	cutaneous use
Austria	Laboratoires Besins International SA Rue de Bourg l'Abbè 3 75003 Paris France	testosterone	Testogel 50 mg - Gel im Beutel	50 mg	gel	cutaneous use
Austria	ProStrakan Ltd. Galabank Business Park TD1 1QH Galashiels United Kingdom	testosterone	Tostran 2% - Gel	0.02	gel	cutaneous use
Austria	Laboratoires Besins International SA Rue de Bourg l'Abbè 3 75003 Paris France	testosterone	Androgel 25 mg - Gel im Beutel	25 mg	gel	cutaneous use
Austria	Laboratoires Besins International SA Rue de Bourg l'Abbè 3 75003 Paris France	testosterone	Androgel 50 mg - Gel im Beutel	50 mg	gel	cutaneous use

Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Austria	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoat	Andriol Testocaps 40 mg - Kapseln	40 mg	capsule, soft	oral use
Belgium	Besins Healthcare Avenue Louise 287 1050 Brussels Belgium	testosterone	Androgel	25 mg	gel	transdermal use
Belgium	Besins Healthcare Avenue Louise 287 1050 Brussels Belgium	testosterone	Androgel	50 mg	gel	transdermal use
Belgium	Eli Lilly Benelux S.A.-N.V. Rue du Marquis 1 1000 Brussels Belgium	testosterone	Axxeron	30 mg/1,5 ml	cutaneous solution	cutaneous use
Belgium	ProStrakan Ltd. Galabank Business Park TD1 1QH Galashiels Selkirkshire United Kingdom	testosterone	Itrogen	2%	gel	cutaneous use
Belgium	Bayer SA-NV Jan Emiel Mommaertsiaan 14 1831 Machelen Belgium	testosterone undecylate	Nebido	1000 mg/4 ml	solution for injection	intramuscular use
Belgium	Aspen Pharma Trading Limited, 3016 Lake Drive Citywest Business Campus Dublin 24 Ireland	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Sustanon 250	30 mg/ml 60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use

Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Belgium	Ferring SA-NV Capucienenlaan 93C 9300 Aalst Belgium	testosterone	Testim	50 mg	gel	transdermal use
Belgium	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoate	Testocaps	40 mg	capsule, soft	oral use
Belgium	Besins Healthcare Avenue Louise 287 1050 Brussels Belgium	testosterone	Testogel	25 mg	gel	transdermal use
Belgium	Besins Healthcare Avenue Louise 287 1050 Brussels Belgium	testosterone	Testogel	50 mg	gel	transdermal use
Bulgaria	Ferring GmbH Wittland 11 + Kiel D-24109 Germany	testosterone	Testim	50 mg	gel	transdermal use
Bulgaria	PharmaSwiss Ceska republika s.r.o. Jankovcova 1569/2c + Praha 17000 Czech Republic	testosteron decanoate testosteron isocaproate testosteron phenylpropionate testosteron propionate	Omnadren	100 mg/ml 60 mg/ml 60 mg/ml 30 mg/ml	solution for injection	intramuscular use
Bulgaria	Bayer Pharma AG Müllerstraße 178 D-13353 Berlin Germany	testosteron undecanoate	Nebido	250 mg/ml	solution for injection	intramuscular use

Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Bulgaria	Laboratoires Besins International rue du Bourg I 75003 Paris France	testosterone	Androgel	50 mg	gel	transdermal use
Czech Republic	BB Pharma a.s. Pod višňovkou 1662/21 140 00 Praha 4 Czech Republic	testosterone isobutyrate	Agovirin depot	25 mg/ml	suspension for injection	intramuscular use
Czech Republic	Laboratoires Besins-International rue du Bourg-I´Abbé 5 75003 Paris France	testosterone	Androgel 25 mg, gel v sáčku	10 mg/g	gel	cutaneous use
Czech Republic	Laboratoires Besins-International rue du Bourg-I´Abbé 5 75003 Paris France	testosterone	Androgel 50 mg, gel v sáčku	10 mg/g	gel	cutaneous use
Czech Republic	BB Pharma a.s. Pod višňovkou 1662/21 140 00 Praha 4 Czech Republic	testosterone isobutyrate estradiol benzoate	Folivirin	25 mg/ml 2,5 mg/ml	suspension for injection	intramuscular use
Czech Republic	Bayer Pharma AG Müllerstrasse 178 13353 Berlin Germany	testosterone undecanoate (testosterone)	Nebido	1000 mg (631,6 mg)	solution for injection	intramuscular use
Czech Republic	Aspen Pharma Trading Limited 3016 Lake Drive Citywest Business Campus Dublin 24 Ireland	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Sustanon 250	30 mg/ml  60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use

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Czech Republic	FERRING Pharmaceuticals CZ s.r.o. K Rybníku 475 252 42 Jesenice u Prahy Czech Republic	testosterone	Testim 50 mg gel transdermální gel	10 mg/g	gel	transdermal use
Czech Republic	N.V. Organon 6 Kloosterstraat 5340 BH Oss The Netherlands	testosterone undecanoate	Undestor	40 mg	capsule, soft	oral use
Croatia	Bayer d.o.o. Radnička cesta 80/8 Zagreb 10000 Croatia	testosteronum undecanoatum	Nebido 1000 mg/4 ml otopina za injekciju	1000 mg/4 ml	solution for injection	intramuscular use
Croatia	Hospitalija trgovina d.o.o. Vojvodići 25, Novaki Sveta Nedelja 10431 Croatia	testoteronum	Androgel 50 mg, gel u vrećici	50 mg	gel	cutaneous use
Cyprus	Bayer Hellas ABEE 18-20 Sorou Street Marousi Athens 15125 Greece	testosterone undecanoate	Nebido	1000 mg/4ml	solution for injection	intramuscular use
Cyprus	Ferring Hellas MEPE 3 Gkyzi street Marousi 15125 Greece	testosterone	Testim	50mg	gel	cutaneous transdermal use



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Cyprus	Laboratoires Besins International 3 Rue du Bourg l' Abbe Paris 75003 France	testosterone	Testogel	25 mg	gel	cutaneous transdermal use
Cyprus	Laboratoires Besins International 3 Rue du Bourg l' Abbe Paris 75003 France	testosterone	Testogel	50mg	gel	cutaneous transdermal use
Denmark	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoate	Andriol	40 mg	capsule, soft	oral use
Denmark	Laboratoires Besins Int., 3 rue du Bourg l'Abbé 75003 Paris France	testosterone	Androgel	25 mg/dose	gel in sachet- dose	transdermal use
Denmark	Laboratoires Besins Int. 3 rue du Bourg l'Abbé 75003 Paris France	testosterone	Androgel	50 mg/dose	gel in sachet- dose	transdermal use
Denmark	Eli Lilly Danmark A/S Lyskær 3E, 2.tv. DK-2730 Herlev Denmark	testosterone	Axiron	2%	cutaneous solution	cutaneous use
Denmark	Bayer Pharma AG Müllerstrasse 170-178 DE-13342 Berlin Germany	testosterone	Nebido	1000 mg/dose	solution for injection	intramuscular use

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Denmark	Ferring Lægemedler A/S, Kay Fiskers Plads 11 DK-2300 København S Denmark	testosterone	Testim	50 mg/dose	gel	transdermal use
Denmark	Laboratoires Besins Int. 3 rue du Bourg l'Abbé 75003 Paris France	testosterone	Testogel	50 mg/dose	gel in sachet-dose	transdermal use
Denmark	Laboratoires Besins Int. 3 rue du Bourg l'Abbé 75003 Paris France	testosterone	Testogel	25 mg/dose	gel in sachet-dose	transdermal use
Denmark	ProStrakan Ltd. Galabank Business Park TD1 1QH Galashiels United Kingdom	testosterone	Tostran	2%	gel	cutaneous use
Estonia	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	SUSTANON	30 mg/ml 60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use
Estonia	Bayer Pharma AG - 13342 Berlin Germany	testosterone	NEBIDO	250 mg/ml	solution for injection	intramuscular use
Estonia	Ferring Lääkkeet Oy PL 23, 02241 Espoo Finland	testosterone	TESTIM 50 MG GEL	50 mg	gel	transdermal use

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Finland	Oy Eli Lilly Finland Ab Laajalahdentie 23 FI- 00330 Helsinki Finland	testosterone	AXIRON	30 mg/1.5 ml	cutaneous solution	transdermal use
Finland	Bayer Oy Pansiontie 47 PL 415 20101 Turku Finland	testosterone undecanoate	NEBIDO	1000 mg/4ml	solution for injection	intramuscular use
Finland	N.V. Organon PO BOX 20 5340 BH Oss The Netherlands	testosterone undecanoate	PANTESTON	40 mg	capsule, soft	oral use
Finland	Aspen Pharma Trading Limited 3016 Lake Drive Citywest Business Campus Dublin 24 Ireland	testosterone propionate testosterone phenylpropionate testosterone isocaproate, testosterone decanoate	SUSTANON"250"	30 mg/ml 60 mg/ml 60mg/ml 100 mg/ml	solution for injection	intramuscular use
Finland	Ferring Lääkkeet Oy Piispansilta 11 A PL 23 02241 Espoo Finland	testosterone	TESTIM	50 mg	gel	transdermal use
Finland	Laboratoires Besins 3, rue du Bourg l'Abbe75003 Paris France	testosterone	TESTOGEL	25 mg/dose	gel	transdermal use

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Finland	Laboratoires Besins 3, rue du Bourg l'Abbe75003 Paris France	testosterone	TESTOGEL	50 mg/dose	gel	transdermal use
Finland	ProStrakan Ltd. Galabank Business Park Galashiels, Selkirkshire TD1 1QH United Kingdom	testosterone	TOSTRAN	2%	gel	transdermal use
France	LABORATOIRES BESINS INTERNATIONAL 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	ANDROGEL 25 mg, gel en sachet-dose	25 mg/2,5 g	gel	transdermal use
France	LABORATOIRES BESINS INTERNATIONAL 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	ANDROGEL 50 mg, gel en sachet-dose	50 mg/5 g	gel	transdermal use
France	BAYER SANTE 220, avenue de la Recherche, 59120 Loos France	testosterone enantate	ANDROTARDYL 250 mg/1 ml, solution injectable intramusculaire	250 mg/ml	solution	intramuscular use
France	PROSTRAKAN Ltd Galabank Business Park TD1 1QH Galashiels United Kingdom	testosterone	FORTIGEL 2 %, gel	20 mg/g	gel	cutaneous use
France	BAYER SANTE 220, avenue de la Recherche 59120 Loos France	testosterone undecanoate	NEBIDO 1000 mg/4 ml, solution injectable	1000 mg/4 ml	Solution	intramuscular use

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France	MSD France 34, avenue Léonard de Vinci 92400 Courbevoie France	testosterone undecanoate	PANTESTONE 40 mg, capsule molle	40 mg	capsule, soft	oral use
France	LABORATOIRES BESINS INTERNATIONAL 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	TESTOGEL 25 mg, gel en sachet-dose	25 mg /2,5 g unidose	gel	transdermal use
France	LABORATOIRES BESINS INTERNATIONAL 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	TESTOGEL 50 mg, gel en sachet-dose	50 mg/5 g unidose	gel	transdermal use
France	Pierre FABRE MEDICAMENT 45, place Abel Gance, 92100 Boulogne Billancourt France	testosterone	TESTOPATCH 1,2 mg/24 heures, dispositif transdermique	15 mg/patch	patch	transdermal use
France	Pierre FABRE MEDICAMENT 45, place Abel Gance, 92100 Boulogne Billancourt France	testosterone	TESTOPATCH 1,8 mg/24 heures, dispositif transdermique	22,5 mg/patch	patch	transdermal use
France	Pierre FABRE MEDICAMENT 45, place Abel Gance 92100 Boulogne Billancourt France	testosterone	TESTOPATCH 2,4 mg/24 heures, dispositif transdermique	30 mg/patch	patch	transdermal use

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France	FERRING SAS 7, rue Jean-Baptiste Clément 94250 Gentilly France	testosterone	TESTIMED 1 %, gel en récipient unidose	50 mg/5 g unidose	gel	transdermal use
Germany	Dr. August Wolff GmbH&Co. KG Arzneimittel Sudbrackstr. 56 33611 Bielefeld Germany	testosterone	Testotop Gel 125mg	125 mg/5g	gel	cutaneous use
Germany	Dr. August Wolff GmbH&Co. KG Arzneimittel Sudbrackstr. 56 33611 Bielefeld Germany	testosterone	Testotop Gel 62,5mg	62,5 mg/2,5g	gel	cutaneous use
Germany	Eifelfango Chemisch- Pharmazeutische Wrke GmbH&Co. KG Ringener Str. 45 53474 Bad Neuenahr- Ahrweiler Germany	testosterone enantate	Testosteron-Depot 250mg Eifelfango	250 mg/1ml	solution for injection	intramuscular use
Germany	Ferring Arzneimittel GmbH Fabrikstr.7 24103 Kiel Germany	testosterone	Testim 50mg Transdermales Gel	50 mg/5g	gel	cutaneous use
Germany	GALENpharm GmbH Wittland13 24109 Kiel Germany	testosterone enantate	Testosteron-Depot GALEN 250mg	250 mg/ml	solution for injection	intramuscular use

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Germany	Jenapharm GmbH&CO. KG Otto-Schott-Str.15 07745 Jena Germany	testosterone undecanoate	Nebido 1000mg Injektionslösung	250 mg/ml	solution for injection	intramuscular use
Germany	Jenapharm GmbH&CO. KG Otto-Schott-Str.15 07745 Jena Germany	testosterone enantate	Testosteron-Depot Jenapharm	250 mg/ml	solution for injection	intramuscular use
Germany	Jenapharm GmbH&CO. KG Otto-Schott-Str.15 07745 Jena Germany	testosterone enantate	Testoviron-Depot Jenapharm	250 mg/ml	solution for injection	intramuscular use
Germany	Jenapharm GmbH&CO. KG Otto-Schott-Str.15 07745 Jena Germany	testosterone enantate	Testoviron-Depot-250	250 mg/ml	solution for injection	intramuscular use
Germany	Laboratoires Besins international 3 rue du Bourgl Abbe 75003 Paris France	testosteron	Androtop Gel 25mg	25 mg/2,5g	gel	cutaneous use
Germany	Laboratoires Besins international 3 rue du Bourgl Abbe 75003 Paris France	testosterone	Androtop Gel 50mg	50 mg/5g	gel	cutaneous use
Germany	Laboratoires Besins international 3 rue du Bourgl Abbe 75003 Paris France	testosterone	Testogel 25mg Gel im Beutel	25 mg/2,5g	gel	cutaneous use

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Germany	Laboratoires Besins international 3 rue du Bourgl Abbe 75003 Paris France	testosterone	Testogel 50mg Gel im Beutel	50 mg/5g	gel	cutaneous use
Germany	Lilly Deutschland GmbH Teichweg 3 35396 Gießen Germany	testosterone	Axiron 30mg/1,5ml Lösung zur Anwendung auf der Haut	30 mg/1,5ml	solution	cutaneous use
Germany	MSD Sharp&Dohme Gesellschaft mit beschränkter Haftung Lindenplatz 1 85540 Haar Germany	testosterone undecanoate	Andriol Testocaps	40 mg	capsule	oral use
Germany	Pierre Faber Pharma GmbH Jechtlinger Str. 13 79111 Freiburg Germany	testosterone	Testopatch 1,2mg/24h, transdermales Pflaster	15 mg	transdermal patch	transdermal use
Germany	Pierre Faber Pharma GmbH Jechtlinger Str. 13 79111 Freiburg Germany	testosterone	Testopatch 1,8mg/24h, transdermales Pflaster	22.5 mg	transdermal patch	transdermal use
Germany	Pierre Faber Pharma GmbH Jechtlinger Str. 13 79111 Freiburg Germany	testosterone	Testopatch 2,4mg/24h, transdermales Pflaster	30 mg	transdermal patch	transdermal use



<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Germany	ProStrakan Limited Galabank Business Park TD1 QH Galashiels United Kingdom	testosterone	Tostran 2% Gel	20 mg/g	gel	cutaneous use
Germany	Rotexmedica GmbH Arzneimittelwerk Bunsenstr.4 22946 Trittau Germany	testosterone enantate	Testosteron Depot- Rotexmedica	250 mg/ml	solution for injection	intramuscular use
Greece	Laboratoires Besins Internationales, Paris, France 5, rue de Bourg l' Abbe 75003 Paris France	testosterone	Testogel	25 mg/sachet	gel	cutaneous use
Greece	Laboratoires Besins Internationales, Paris, France 5, rue de Bourg l' Abbe 75003 Paris France	testosterone	Testogel	50 mg/sachet	gel	cutaneous use
Greece	Ferring Ellas Farmakeytiki MEPE Gyzi 3 15125 Marousi Greece	testosterone	Testim	1% (w/w)	gel	cutaneous use
Greece	Prostrakan Ltd, U.K. Galabank Business Park Galashiels, TD1 1QH United Kingdom	testosterone	Tostran	2% (w/w)	gel	cutaneous use
Greece	Pierre Fabre Farmaka AE I. Mesogion 350, 15341 Ag. Paraskevi Greece	testosterone	Testopatch	1.2 mg/24h	transdermal patch	cutaneous use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Greece	Pierre Fabre Farmaka AE I. Mesogion 350 15341 Ag. Paraskevi Greece	testosterone	Testopatch	1.8 mg/24h	transdermal patch	cutaneous use
Greece	Pierre Fabre Farmaka AE I. Mesogion 350 15341 Ag. Paraskevi Greece	testosterone	Testopatch	2.4 mg/24h	transdermal patch	cutaneous use
Greece	Bayer Ellas ABEE Sorou 18-20 15125 Marousi Greece	testosterone enantate	Testoviron	250 mg/ml	solution for injection	intramuscular use
Greece	Norma Ellas AE Menandrou 54 10431 Athens Greece	testosterone enantate	Testosterone Enenthate/Norma	250 mg/ml	solution for injection	intramuscular use
Greece	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoate	Restandol Testocaps	40 mg	capsules, soft	oral use
Greece	Bayer Ellas ABEE Sorou 18-20 15125 Marousi Greece	testosterone undecanoate	Nebido	1000 mg/4ml	solution for injection	intramuscular use
Hungary	N.V. Organon Postbus 20 5340 BH Oss The Netherlands	testosterone undecanoate	Andriol Testocaps 40 mg lágy kapszula	40 mg	capsule, soft	oral use
Hungary	Laboratoires Besins International 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	Androgel 25 mg gél tasakban	25 mg	gel	cutaneous use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Hungary	Laboratoires Besins International 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	Androgel 50 mg gél tasakban	50 mg	gel	cutaneous use
Hungary	Bayer Pharma AG Müllerstrasse 178 D-13342 Berlin Germany	testosterone	Nebido 250 mg/ml oldatos injekció	250 mg/ml	solution for injection	intramuscular injection
Hungary	Ferring Magyarország Gyógyszerkereskedelmi Kft. Tomori u. 34. Budapest H-1138 Hungary	testosterone	Testim 50 mg transzdermális gél	50 mg	gel	cutaneous use
Hungary	ProStrakan Limited Galabank Business Park Galashiels, TD1 1QH United Kingdom	testosterone	Tostran 20 mg/g gél	20 mg/g	gel	cutaneous use
Iceland	Laboratories BESINS INTERNATIONAL 3, rue du Bourg 1'Abbé 75003 Paris France	testosteronum	Androgel	50 mg/dosage	gel	cutaneous use
Iceland	Laboratories BESINS INTERNATIONAL 3, rue du Bourg 1'Abbé 75003 Paris France	testosteronum	Testogel	25 mg/dosage	gel	cutaneous use
Iceland	Laboratories BESINS INTERNATIONAL 3, rue du Bourg 1'Abbé 75003 Paris France	testosteronum	Testogel	50 mg/dosage	gel	cutaneous use

Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Iceland	Ferring Lægemedler A/S (F) Kay Fiskers Plads 11. 2300 København S Denmark	testosteronum	Testim	50 mg/dosage	gel	cutaneous use
Iceland	Bayer Pharma AG Müllerstrasse 178 13353 Berlin Germany	testosteronum undecanoat	Nebido	250 mg/ml	solution for injection	intramuscular use
Italy	Laboratorio Farmaceutico SIT Speciatilta' Igienico Terapeutiche S.R.L. Via Cavour, 70 Mede 27035 Pavia Italy	testosterone propionate	TESTOVIS	100mg/2ml	solution for injection	intramuscular use
Italy	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	SUSTANON	30 mg/ml 60 mg/ml 60mg/ml 100 mg/ml	solution for injection	intramuscular use
Italy	BAYER S.P.A. Viale Certosa, 130 20156 Milano Italy	testosterone enanthate	TESTOVIRON	250 mg/ml	solution for injection	intramuscular use
Italy	GEYMONAT S.P.A. Via S. Anna, 2 03012 Anagni Frosinone Italy	testosterone enanthate	TESTO ENANT	100 mg/ml	solution for injection	intramuscular use

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Italy	GEYMONAT S.P.A., Via S. Anna, 2 03012 Anagni Frosinone Italy	testosterone enanthate	TESTO ENANT	250 mg/2ml	solution for injection	intramuscular use
Italy	BAYER S.P.A., Viale Certosa, 130 20156 Milano Italy	testosterone undecanoate	NEBID	1000 mg/4ml	solution for injection	intramuscular use
Italy	MSD ITALIA S.R.L. Via Vitorchiano 151 00189 Roma Italy	testosterone undecanoate	ANDRIOL	40 mg	capsules	oral use
Ireland	Laboratoires BESINS INTERNATIONAL, 3 Rue du Bourg l'Abbé 75003 Paris France	testosterone	Androgel 25 mg, gel in sachet	25 mg	gel	cutaneous use
Ireland	Laboratoires BESINS INTERNATIONAL 3 Rue du Bourg l'Abbé 75003 Paris France	testosterone	Androgel 50 mg, gel in sachet	50 mg	gel	cutaneous use
Ireland	Laboratoires BESINS INTERNATIONAL 3 Rue du Bourg l'Abbé 75003 Paris France	testosterone	Testogel 25 mg, gel in sachet	25 mg	gel	cutaneous use
Ireland	Laboratoires BESINS INTERNATIONAL 3 Rue du Bourg l'Abbé 75003 PARIS France	testosterone	Testogel 50 mg, gel in sachet	50 mg	gel	cutaneous use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Ireland	ProStrakan Ltd. Galabank Business Park Galashiels TD1 1QH United Kingdom	testosterone	Tostran 2% Gel	2% w/w (20mg testosterone per 1g gel)	gel	cutaneous use
Ireland	Ferring Ireland Ltd United Drug House Magna Drive Magna Business Park Citywest Road Dublin 24 Ireland	testosterone	Testim 50mg Gel	50 mg	gel	cutaneous use
Ireland	Organon (Ireland) Limited PO Box 2857, Drynam Road, Swords Co. Dublin Ireland	testosterone undecanoate	Restandol Testocaps	40 mg	capsules, soft	oral use
Ireland	Bayer Limited The Atrium Blackthorn Road Dublin 18 Ireland	testosterone undecanoate	Nebido 1000 mg/4ml, solution for injection	250 mg/ml	solution for Injection	intramuscular
Latvia	Ferring Laakkeet Oy Piispansilta 11 A 02230 Espoo Finland	testosterone	Testim 50 mg transdermal gel	50 mg	gel	transdermal use
Latvia	PharmaSwiss Česká republika s.r.o. Jankovcova 1569/2c 170 00 Prague 7 Czech Republic	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Omnadren 250 mg/ml solution for injection	30 mg/ml  60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Latvia	Laboratoires BESINS INTERNATIONAL 3, rue duBourg l'Abbe 75003 Paris France	testosterone	Androgel 25 mg gel in sachet	25 mg	gel in sachet	cutaneous use
Latvia	Laboratoires BESINS INTERNATIONAL 3, rue duBourg l'Abbe 75003 PARIS France	testosterone	Androgel 50 mg gel in sachet	50 mg	gel in sachet	cutaneous use
Latvia	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Sustanon 250 mg/ml solution for injection	30 mg/ml 60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use
Latvia	Bayer Pharma AG D-13342 Berlin Germany	testosterone undecanoate	Nebido 1000 mg/4 ml solution for injection	1000 mg/4 ml	solution for injection	intramuscular use
Lithuania	Bayer Pharma AG Mullerstrasse 178 D-13342 Berlin Germany	testosterone undecanoate	Nebido	1000 mg/4 ml	solution for injection	intramuscular use
Lithuania	N.V. ORGANON P.O. Box 20 5340 BH Oss The Netherlands	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Sustanon	30 mg/ml 60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Lithuania	Ferring Lääkkeet Oy PL 23 02241 Espoo Finland	testosterone	Testim	50 mg	gel	transdermal use
Luxembourg	Besins International S.A. 3, rue du Bourg l'Abbe 75003 Paris France	testosterone	Androgel	25 mg/2,5 g	gel	cutaneous use
Luxembourg	Besins International S.A. 3, rue du Bourg l'Abbe 75003 Paris France	testosterone	Androgel	50 mg/5 g	gel	cutaneous use
Luxembourg	Eli Lilly Benelux S.A. -N.V 1, rue du Marquis 1000 Bruxelles Belgium	testosterone	Axxeron	30 mg/1,5 ml	transdermal spray, solution	cutaneous use
Luxembourg	Prostrakan Ltd Galabank Business Park Galashiels TD1 1QH United Kingdom	testosterone	Itrogen	2 g/100 g	gel	cutaneous use
Luxembourg	Bayer S.A.-N.V. 14, J.E.Mommaerstlaan 1831 Diegem (Machelen) Belgium	testosterone undecanoate	Nebido	250 mg/ml	solution for injection	intramuscular use



Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Luxembourg	Aspen Pharma Trading Limited, 3016 Lake Drive, Citywest Business Campus, Dublin 24, Ireland	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Sustanon	30 mg/ml 60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use
Luxembourg	Ferring S.A. 93C, Capucienenlaan 9300 Aalst Belgium	testosterone	Testim	50 mg/5 g	gel	cutaneous use
Luxembourg	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoate	Testocaps	40 mg	capsule, soft	oral use
Luxembourg	Besins International S.A. 3, rue du Bourg l'Abbe 75003 Paris France	testosterone	Testogel	25 mg/2,5 g	gel	cutaneous use
Luxembourg	Besins International S.A. 3, rue du Bourg l'Abbe 75003 Paris France	testosterone	Testogel	50 mg/5 g	gel	cutaneous use
Malta	Bayer plc Bayer House Strawberry Hill Newbury Berkshire RG14 1JA United Kingdom	testosterone undecanoate	Nebido	250 mg/ml	solution for injection	intramuscular use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Malta	Ferring Pharmaceuticals Limited Drayton Hall Church Road West Drayton UB7 7PS United Kingdom	testosterone	Testim 50mg Transdermal Gel	50 mg/5g	gel	transdermal use
The Netherlands	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosteronundecanoaat	Andriol Testocaps, 40 mg capsules	40,0 mg	capsule, soft	oral use
The Netherlands	Laboratoires Besins International 3, rue du Bourg l'Abbé Paris 75003 France	testosteron	Androgel 25 mg, gel in sachet	25,0 mg/sachet	gel	cutaneous use
The Netherlands	Laboratoires Besins International 3, rue du Bourg l'Abbé Paris 75003 France	testosteron	Androgel 50 mg, gel in sachet	50 mg/sachet	gel	cutaneous use
The Netherlands	Bayer B.V. Energieweg 1 3641 RT Mijdrecht The Netherlands	testosteronundecanoaat	Nebido 1000 mg/4 ml, oplossing voor injectie	250,0 mg/ml	solution for injection	intramuscular use
The Netherlands	Aspen Pharma Trading Limited 3016 Lake Drive Citywest Business Campus Dublin 24 Ireland	testosteron: testosterone isocaproate testosteron phenylpropionate testosterone propionate	Sustanon 100 mg/ml, oplossing voor injectie	74,0 mg/ml: 40 mg/ml 40 mg/ml 20 mg/ml	solution for injection	intramuscular use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
The Netherlands	Aspen Pharma Trading Limited 3016 Lake Drive Citywest Business Campus Dublin 24 Ireland	testosteron: testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Sustanon 250 mg/ml, oplossing voor injectie	176,1 mg/ml: 30 mg/ml 60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use
The Netherlands	Ferring B.V. Polarisavenue 130 2132 JX Hoofddorp The Netherlands	testosteron	Testim 50 mg gel, gel 50 mg/tube	50 mg	gel	cutaneous use
The Netherlands	Laboratoires Besins International 3, rue du Bourg l'Abbé Paris 75003 France	testosteron	Testogel 25 mg, gel in sachet	25 mg	gel	cutaneous use
The Netherlands	Laboratoires Besins International 3, rue du Bourg l'Abbé Paris 75003 France	testosteron	Testogel 50 mg, gel in sachet	50 mg	gel	cutaneous use
The Netherlands	ProStrakan Ltd Galabank Business Park Galashiels TD1 1QH United Kingdom	testosteron	Tostran 2% gel, gel 0,02 g/g	0,02 g/g	gel	cutaneous use
Norway	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoate	Andriol	40 mg	capsule, soft	oral use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Norway	Eli Lilly Norge AS P.B. 6090 Etterstad N-0601 Oslo Norway	testosterone	Axiron	20mg/ml	cutaneous solution	transdermal use
Norway	Bayer Pharma AG, Müllerstrasse 178 03353 Berlin Germany	testosterone undecanoate	Nebido	1000 mg/4ml	solution for injection	parenteral use
Norway	Ferring Legemidler AS Nydalsveien 36B 0484 Oslo Norway	testosterone	Testim	50 mg/5g	gel	transdermal use
Norway	Laboratoires Besins International 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	Testogel	25 mg/2,5g	gel	transdermal use
Norway	Laboratoires Besins International 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	Testogel	50 mg/5g	gel	transdermal use
Norway	ProStrakan Ltd Galabank Business Park Galashiels, TD1 1PR United Kingdom	testosterone	Tostran	2%	gel	transdermal use
Poland	Laboratoires Besins International 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	Androtop	25 mg/2,5 g	gel	cutaneous use

Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Poland	Bayer Pharma AG Müllerstrasse 178 13353 Berlin Germany	testosterone undecanoate	Nebido	1000 mg/4 ml	solution for injection intramuscular	intramuscular use
Poland	PharmaSwiss Ceska Republika s.r.o. Jankovcova 1569/2c + Praha 17000 Czech Republic	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Omnadren 250	30 mg/ml 60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use
Poland	Ferring GmbH Wittland 11, D-24109 Kiel Germany	testosterone	Testim	50 mg	gel	cutaneous use
Poland	PharmaSwiss Ceska Republika s.r.o. Jankovcova 1569/2c + Praha 17000 Czech Republic	testosterone enantane	Testosteronum prolongatum Jelfa	100 mg/ml	solution for injection	intramuscular use
Poland	ProStrakan Limited Galabank Business Park TD1 QH Galashiels United Kingdom	testosterone	Tostran 2% žel	2%	gel	cutaneous use
Poland	N.V. ORGANON Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoate	Undestor Testocaps	40 mg	capsule	oral use

Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Portugal	Merck Sharp & Dohme, Lda. Quinta da Fonte - Edifício Vasco da Gama, 19 - Porto Salvo 2770-192 Paço d' Arcos Portugal	testosterone undecanoate	Andriol - T	40 mg	capsule, soft	oral use
Portugal	Besins International, S.A. 5, Rue du Bourg l'Abbé F-75003 Paris France	testosterone	Androgel	25 mg/2.5 g	gel	cutaneous use
Portugal	Besins International, S.A. 5, Rue du Bourg l'Abbé F-75003 Paris France	testosterone	Androgel	50 mg/5 g	gel	cutaneous use
Portugal	Bayer Portugal, S.A. Rua Quinta do Pinheiro, 5 2794-003 Carnaxide Portugal	testosterone undecanoate	Nebido	1000 mg/4 ml	solution for injection	intramuscular use
Portugal	Aspen Pharma Trading Limited. 3016 Lake Drive. Citywest business campus. Dublin 24. Ireland	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Sustenon	30 mg/ml 60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use
Portugal	Ferring Portuguesa - Produtos Farmacêuticos, Sociedade Unipessoal, Lda. Rua Alexandre Herculano - Edifício 1, Piso 6 2795-240 Linda-a-Velha Portugal	testosterone	Testim	50 mg/5 g	gel	transdermal use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Portugal	Besins International, S.A. 5, Rue du Bourg l'Abbé F-75003 Paris France	testosterone	Testogel	25 mg/2.5 g	gel	cutaneous use
Portugal	Besins International, S.A. 5, Rue du Bourg l'Abbé F-75003 Paris France	testosterone	Testogel	50 mg/5 g	gel	cutaneous use
Portugal	Pierre Fabre Médicament Portugal, Lda. Rua Rodrigo da Fonseca 178 - 2º Esq 1099-067 Lisboa Portugal	testosterone	Testopatch	1.2 mg/24 h	transdermal patch	transdermal use
Portugal	Pierre Fabre Médicament Portugal, Lda. Rua Rodrigo da Fonseca 178 - 2º Esq 1099-067 Lisboa Portugal	testosterone	Testopatch	1.8 mg/24 h	transdermal patch	transdermal use
Portugal	Pierre Fabre Médicament Portugal, Lda. Rua Rodrigo da Fonseca 178 - 2º Esq 1099-067 Lisboa Portugal	testosterone	Testopatch	2.4 mg/24 h	transdermal patch	transdermal use
Portugal	Bayer Portugal, S.A. Rua Quinta do Pinheiro, 5 2794-003 Carnaxide Portugal	testosterone enantate	Testoviron Depot	250 mg/1 ml	solution for injection	intramuscular use

Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Portugal	ProStrakan Limited Galabank Business Park TD1 1QH Galashiels United Kingdom	testosterone	Tostran	20 mg/g	gel	cutaneous use
Romania	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoate	UNDESTOR TESTOCAPS 40 mg, capsule moi	40 mg	capsules soft	Oral use
Romania	BAYER PHARMA AG Müllerstraße 178 13353 Berlin Germany	testosterone undecanoat	NEBIDO 1000 mg/4 ml	1000 mg/4 ml	solution for injection	intramuscular use
Romania	LABORATOIRES BESINS INTERNATIONAL 3, rue de Bourg L'Abbé 75003 Paris France	testosterone	ANDROGEL 50 mg	50 mg/5 g	gel	cutaneous use
Romania	Ferring GmbH Wittland 11, D-24109 Kiel Germany	testosterone	TESTIM 50 mg	50 mg/5 g	gel	cutaneous use
Slovak Republic	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoate	Undestor Testocaps 40 mg	40 mg	capsule, soft	oral use
Slovak Republic	Bayer Pharma AG Müllerstr. 178 13353 Berlin Germany	testosterone	Nebido 1000 mg/4 ml injekčný roztok	250 mg/ml	solution for injection	intramuscular use



Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Slovak Republic	Aspen Pharma Trading Limited 3016 Lake Drive Citywest Business Campus Dublin 24 Ireland	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Sustanon 250	30 mg/ml 60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use
Slovak Republic	BB Pharma a.s. Pod Višňovkou 1662/21 14000 Praha 4 Czech Republic	testosterone	AGOVIRIN DEPOT	5 mg/2 ml	suspension for injection	intramuscular use
Slovak Republic	BB Pharma a.s. Pod Višňovkou 1662/21 14000 Praha 4 Czech Republic	estradiol/testosterone	FOLIVIRIN	2,5 mg/25 mg/ ml	suspension for injection	intramuscular use
Slovak Republic	Ferring-Léčiva, a.s. K Rybníku 475 252 42 Jesenice u Prahy Czech Republic	testosterone	Testim 50 mg gél	50 mg/5 g	transdermal gel	transdermal use
Slovenia	Ferring GmbH Wittland 11 24109 Kiel Germany	testosterone	TESTIM 50 mg transdermalni gel	50 mg	transdermal gel	transdermal use
Slovenia	Bayer Pharma AG 13342 Berlin Germany	testosterone	Nebido 1000 mg/4 ml raztopina za injiciranje	1000 mg/4 ml	Solution for injection	intramuscular use
Slovenia	Laboratoires BESINS INTERNATIONAL 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	Androtop 50 mg gel v blazinici	50 mg	gel in sachet	transdermal use

Member State (in EEA)	Marketing authorisation holder	INN	Invented name	Strength	Pharmaceutical form	Route of administration
Slovenia	Laboratoires BESINS INTERNATIONAL 3, rue du Bourg l'Abbé 75003 Paris France	testosterone	Androtop 25 mg gel v blazinici	25 mg	gel in sachet	transdermal use
Spain	DESMA LABORATORIO FARMACÉUTICO, S.L. Cuatro Amigos, 7 Escalera 2, 1ºD 28029 Madrid Spain	testosterone propionate	TESTEX	25 mg/ml	solution for injection	intramuscular use
Spain	DESMA LABORATORIO FARMACÉUTICO, S.L. Cuatro Amigos, 7 Escalera 2, 1ºD 28029 Madrid Spain	testosterone propionate	TESTEX PROLONGATUM 100	100 mg/2 ml	solution for injection	intramuscular use
Spain	DESMA LABORATORIO FARMACÉUTICO, S.L. Cuatro Amigos, 7 Escalera 2, 1ºD 28029 Madrid Spain	testosterone propionate	TESTEX PROLONGATUM 250	250 mg/2 ml	solution for injection	intramuscular use
Spain	BESINS INTERNACIONAL 3, Rue du Bourg l'Abbe 75003 Paris France	testosterone	TESTOGEL 50 mg gel en sobres	1 g/100 g	gel	cutaneous use
Spain	FERRING, S.A.U. Gobelas, 11 Urbanización La Florida 28023 Madrid Spain	testosterone	TESTIM 50 mg gel	1 g/100 g	gel	cutaneous use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Spain	BAYER HISPANIA, S.L. Avda. Baix Llobregat 3 y 5 08970 Sant Joan Despi Barcelona Spain	testosterone undecanoate	REANDRON 1000 mg/4 ml soluci3n inyectable	1000 mg/4 ml	solution for injection	intramuscular use
Spain	PROSTRAKAN LIMITED Galabank Bussines Park Galashield TD1 1QH United Kingdom	testosterone	ITNOGEN 2% gel	2 g/100 g	gel	cutaneous use
Spain	PIERRE FABRE IBERICA S.A. Ram3n Tr3as Fargas, 7-11 08005 Barcelona Spain	testosterone	TESTOPATCH 1,2 mg/24 h parche transd3rmico	1.2 mg/24 h	transdermal patch	cutaneous use
Spain	PIERRE FABRE IBERICA S.A. Ram3n Tr3as Fargas, 7-11 08005 Barcelona Spain	testosterone	TESTOPATCH 1,8 mg/24 h parche transd3rmico	1.8 mg/24 h	transdermal patch	cutaneous use
Spain	PIERRE FABRE IBERICA S.A. Ram3n Tr3as Fargas, 7-11 08005 Barcelona Spain	testosterone	TESTOPATCH 2,4 mg/24 h parche transd3rmico	2.4 mg/24 h	transdermal patch	cutaneous use
Sweden	N.V. Organon Kloosterstraat 6 5349 AB Oss The Netherlands	testosterone undecanoate	Undestor® Testocaps®	40 mg	capsule, soft	oral use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
Sweden	Laboratoires Besins International 3, rue du Bourg l' Abbé FR-75003 Paris France	testosterone	Testogel	25 mg	gel in sachet	cutaneous and transdermal preparations
Sweden	Laboratoires Besins International, 3, rue du Bourg l' Abbé FR-75003 Paris France	testosterone	Testogel	50 mg	gel in sachet	cutaneous and transdermal preparations
Sweden	ProStrakan Ltd, Galabank Business Park Galashiels TD1 1QH United kingdom	testosterone	Tostrex	2%	gel	cutaneous and transdermal preparations
Sweden	Ferring Läkemedel AB Box 4041 203 11 Malmö Sweden	testosterone	Testim	50 mg	gel	cutaneous and transdermal preparations
Sweden	Bayer Pharma AG DE-13342 Berlin Germany	testosterone	Nebido	1000 mg/4 ml	solution for injection	parenteral use
Sweden	Eli Lilly Sweden AB Box 721 169 27 Solna Sweden	testosterone	Axiron	30 mg/1.5 ml	cutaneous solution	cutaneous and transdermal preparations
United Kingdom	Alliance Pharmaceuticals Limited Avonbridge House Bath Road, Chippenham Wiltshire SN15 2BB United Kingdom	testosterone enantate	Testosterone Enantate Ampoules	250 mg/ml	solution for injection	intramuscular use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
United Kingdom	Bayer Plc Bayer House Strawberry Hill, Newbury RG14 1JA United Kingdom	testosterone undecanoate	Nebido 1000mg/4ml, solution for injection	1000 mg/4ml	solution for injection	intramuscular use
United Kingdom	DHP Healthcare Limited 26 Pickering Street Maidstone, Kent ME15 9RS United Kingdom	testosterone propionate	Virormone (100mg/2ml)	100 mg/2ml	solution for injection	intramuscular use
United Kingdom	Ferring Pharmaceuticals Limited Drayton Hall, Church Road West Drayton UB7 7PS United Kingdom	testosterone	Testim 50mg Transdermal Gel	50 mg	gel	transdermal use
United Kingdom	Laboratoires Besins International 5 Rue du Bourg L'Abbe Paris F-75003 France	testosterone	Testogel 50mg. Gel in Sachet	50 mg	gel	cutaneous use
United Kingdom	Merck Sharp & Dohme Limited Hertford Road Hoddesdon Hertfordshire EN11 9BU United Kingdom	testosterone undecanoate	Restandol 40mg	40 mg	capsule	oral use
United Kingdom	Aspen Pharma Trading Limited 3016 Lake Drive Citywest Business Campus Dublin 24 Ireland	testosterone propionate testosterone phenylpropionate testosterone isocaproate testosterone decanoate	Sustanon 250	30 mg/ml  60 mg/ml 60 mg/ml 100 mg/ml	solution for injection	intramuscular use

<b>Member State (in EEA)</b>	<b>Marketing authorisation holder</b>	<b>INN</b>	<b>Invented name</b>	<b>Strength</b>	<b>Pharmaceutical form</b>	<b>Route of administration</b>
United Kingdom	Prostrakan Limited 3 Galabank Business Park Queen Street, Galashiels TD1 1QH United Kingdom	testosterone	Tostran 2% Gel	2% w/w	gel	cutaneous use

## **Annex II**

**Scientific conclusions and grounds for variation to the terms of the marketing authorisations subject to conditions and detailed explanation of the scientific grounds for the differences from the PRAC recommendation**

## Scientific conclusions and detailed explanation of the scientific grounds for the differences from the PRAC recommendation

The CMDh considered the below PRAC recommendation with regard to testosterone containing medicinal products:

### 1 - PRAC recommendation

#### Overall summary of the scientific evaluation by PRAC

Testosterone is an androgenic hormone secreted by the Leydig cells in the testis. It is an essential hormone for the development of male reproductive tissues as the testis and the prostate and in promoting secondary sexual characteristics such as increased muscle, bone mass, and the growth of body hair (*Dollery et al., 1991*<sup>1</sup>).

Hypogonadism in men is a congenital or acquired syndrome, in which the testis fails to produce physiological levels of testosterone and spermatozoa, as there is a disruption in the hypothalamic-pituitary-testicular axis (HPT).

Hypogonadism is classified into primary testicular failure due to a problem in the testicles and secondary testicular failure, due to a problem in the hypothalamus or the pituitary gland. The clinical symptoms depend on the age of onset androgen deficiency. If the hypogonadism develops before puberty e.g. as part of a genetic disease, the men will exhibit eunuchoid proportions, delayed of secondary sex characteristics and high pitched voice. The symptoms are less specific if the hypogonadism develops after puberty and are characterized by e.g. decreased sexual function, infertility, decreased energy, depressed mood, mild anaemia, reduced muscle bulk and strength, increase body fat and BMI (guideline of Endocrine Society).

The major goal of testosterone therapy (TT) is to achieve normal physiological levels of testosterone levels to relieve symptoms of hypogonadism like decreased sexual function, infertility, decreased energy, depressed mood, mild anaemia, reduced muscle bulk and strength, increased body fat and body mass index (BMI) and psychological impairment. There are no treatment alternatives to testosterone for male hypogonadism (*Buvat et al. 2013*<sup>2</sup>).

Testosterone, as well as other androgens and anabolic steroids, should be used cautiously in patients with cardiovascular disorders, renal or hepatic impairment, epilepsy, migraine, diabetes mellitus or other conditions that may be aggravated by the possible fluid retention or oedema caused.

Concerns were raised with regards to a potential increased risk of cardiovascular events, namely myocardial infarction, in men treated with testosterone and who have pre-existing heart disease (*Finkle et al, 2014*<sup>3</sup>; *Vigen et al, 2013*<sup>4</sup> and *Xu et al, 2013*<sup>5</sup>). A referral under Article 31 of Directive

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<sup>1</sup> Dollery C, Boobis AR, Burley D, Davies DM, Davies DS, Harrison PI, Orme ML, Park BK, Goldberg LI eds. Therapeutic drugs. Edinburgh: Churchill Livingstone, 1991; T20-1

<sup>2</sup> Buvat J, Maggi M, Guay A, Torres LO. Testosterone Deficiency in Men: Systematic Review and Standard Operating Procedures for Diagnosis and Treatment. *J Sex Med* 2013; 10: 245–284.

<sup>3</sup> Finkle et al. "Increased risk of non-fatal myocardial infarction following testosterone therapy prescription in men." *PLoS One*. 2014.

<sup>4</sup> Vigen et al. "Association of testosterone therapy with mortality, myocardial infarction, and stroke in men with low testosterone levels." *JAMA*. 2013 Nov 6; 310(17):1829-36.

<sup>5</sup> Xu L, Freeman G, Cowling BJ, Schooling CM. Testosterone therapy and cardiovascular events among men: a systematic review and meta-analysis of placebo-controlled randomized trials. *BMC Med*. 2013; 11:108.



2001/83/EC was therefore initiated, to review the benefit-risk balance of testosterone containing medicinal products.

All testosterone-containing medicinal products approved in the European Union were included in this review performed by the PRAC. All were authorised nationally and are available in different pharmaceutical forms: solution for intramuscular injection, oral capsules, cutaneous gel, cutaneous solution and transdermal patch.

The PRAC reviewed all data available from clinical trials, observational studies, meta-analyses, post-marketing data and further published data on the cardiovascular risks associated with testosterone therapy.

The PRAC acknowledged that some studies show an increased risk of cardiovascular events in men treated with testosterone. The PRAC noted that the findings from several other observational studies, clinical trials and meta-analysis of randomised clinical trials do not provide evidence of an association between testosterone and cardiovascular events. As an example, recently published studies (*Baillargeon et al., 2014<sup>6</sup>; Corona et al., 2014<sup>7</sup>; Tan et al., 2014<sup>8</sup>; Hildreth et al., 2013<sup>9</sup>*), with the objective to examine the risk of cardiovascular events with TT, did not report an increase in this risk. Also, the RHYME study, an observational registry study performed in 6 European countries evaluating the association between TT (over two years) and prostate health outcome in men with hypogonadism also looked at health outcomes, as secondary endpoints. Results suggest that rates of prostate cancer and cardiovascular events were within the anticipated range, with no evidence of increased risk in treated versus untreated patients.

The studies and their limitations were considered together with the overall evidence available to date.

Overall the PRAC concluded that the findings in the literature do not consistently show an increased risk of cardiovascular events and do not corroborate the signal of an increased risk of cardiovascular events associated with testosterone therapy. Therefore, taking the totality of data into account it is judged that the signal for an increased cardiovascular risk associated with the use of testosterone remains weak and inconclusive. It is expected that the marketing authorisation holders continue to monitor cardiovascular events and it is expected that findings of ongoing studies will be reflected in periodic updated safety reports (PSURs) when available. The Committee recognised the limited available information on testosterone therapy for age-related hypogonadism and also the lack of reference. Further studies will be needed to provide relevant safety and efficacy data in this patient population.

It is known that in patients suffering from severe cardiac, hepatic, or renal insufficiency or ischaemic heart disease, treatment with testosterone may cause severe complications characterised by oedema with or without congestive cardiac failure. In such case, treatment must be stopped immediately. The PRAC also recognised that testosterone may have both direct and indirect effect on the cardiovascular systems: low testosterone increases the risk of the metabolic syndrome, which could potentially

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<sup>6</sup> Baillargeon J, Urban RJ, Kuo Y-F, Ottenbacher KJ, Raji MA, Du F, Lin Y-I, Goodwin JS. Risk of myocardial infarction in older men receiving testosterone therapy. *Ann Pharmacother* 2014; 48(9):1138-1144.

<sup>7</sup> Corona G, Maseroli E, Rastrelli G, Isidori A, Mannucci E, Maggi M. Cardiovascular risk associated with testosterone boosting medications: a systematic review and metaanalysis. *Exp Opin Drug Safety* 2014 (Posted online on August 19, 2014. (doi: 10.1517/14740338.2014.950653)

<sup>8</sup> Tan R, Cook KR, Reilly WG. Testosterone therapy is not associated with higher risk of myocardial infarction or stroke: The low T experience. Abstract Book of the 2014 Annual Meeting of the American Association of Clinical Endocrinologists (AACE), pg 238, abstract # 1353; available at: <https://www.aace.com/files/late-breaking-abstracts-2014.pdf>

<sup>9</sup> Hildreth KL, Barry DW, Moreau KL, Vande Griend J, Meacham RB, Nakamura T, Wolfe P, Kohrt WM, Ruscini JM, Kittelson J, Cress ME, Ballard R, Schwartz RS. Effects of testosterone and progressive resistance exercise in healthy, highly functioning older men with low-normal testosterone levels. *J Clin Endocrinol Metab* 2013; 98(5): 1891-1900.

increase the risk of adverse cardiovascular events. On the other hand, testosterone stimulates red blood proliferation, which theoretically could increase the risk of thromboembolic events. Given the knowledge to date, the PRAC recommended that the possible mechanism on the association between cardiovascular/venous thromboembolic events and the level of testosterone be further investigated by the marketing authorisation holders and reported at the next PSUR.

Testosterone should be used with caution in men with hypertension and testosterone levels should be monitored both at baseline and at regular intervals during treatment to ensure the adequacy of the dose administered. In addition, there is limited experience on the safety and efficacy of the use of testosterone in patients over 65 years of age. The marketing authorisation holders are requested to investigate and report in the next PSUR on the usage of these products in this patient population and to consider if the pattern of adverse events is comparable to other age groups.

The next PSUR, will have the common DLP to all testosterone-containing medicinal products of 31 December 2015.

Based on all the above discussed, the PRAC considered justified to reflect in the product information of all testosterone containing medicinal products approved in the European Union that prescribing testosterone for hypogonadism should be based upon confirmation of both clinical features and biochemical testing. Information on the cardiovascular safety and well-documented blood system adverse reactions, which may contribute to the cardiovascular risk should be included in the product information. Also, that there is limited data regarding elderly patients above the age of 65 and this will also be reflected in the warning section of the product information of all testosterone-containing medicinal products.

## Grounds for PRAC recommendation

Whereas

- The PRAC considered the procedure under Article 31 of directive 2001/83/EC for testosterone-containing medicinal products.
- The Committee considered the studies that heightened concerns about the increased risk of cardiovascular events associated with testosterone therapy and available data submitted from clinical trials, observational studies, meta-analyses, post-marketing data and further published data.
- The Committee noted that the available data does not consistently show an increased risk of cardiovascular events during testosterone therapy.
- The PRAC noted that some of the studies have methodological limitations. Some studies show an increased risk while others do not suggest a risk and therefore have not corroborated the signal.
- The PRAC concluded that based on the overall currently available data, the suggested risk for cardiovascular events associated with the testosterone therapy remains a weak signal. The PRAC noted that others studies will become available.
- The Committee recognised the limited available information on testosterone therapy for age-related hypogonadism and also the lack of reference values. Further studies will be needed to provide relevant safety and efficacy data in this patient population.

- The Committee agreed, that it is justified to reflect in the product information of all testosterone-containing medicinal products the current knowledge on cardiovascular risks associated with testosterone therapy and recommended changes in section 4.1 (therapeutic indications), section 4.4 (warnings and precautions for use) and section 4.8 (undesirable effects) of the Summary of Product Characteristics.
- The PRAC also concluded that there was the need for all MAHs to closely monitor cardiovascular risk and discuss the findings including venous thromboembolic events and possible mechanism(s) and usage pattern and adverse events in patients older than 65 years in the next PSUR.

In view of the above, the PRAC has recommended the variation to the terms of the Marketing Authorisations for testosterone-containing medicinal products (see Annex I), for which the relevant sections of the Summary of Product Characteristics and Package Leaflet are set out in Annex III and subject to the conditions set out in Annex IV of the PRAC recommendation.

The PRAC, as a consequence, concluded that the benefit-risk balance of testosterone-containing medicinal products remains favourable subject to the conditions to the marketing authorisations, and taking into account the amendments to the product information recommended.

## **2 – Detailed explanation of the scientific grounds for differences from the PRAC recommendation**

Having reviewed the PRAC recommendation, the CMDh agreed with the overall scientific conclusions and grounds for recommendation.

However, the CMDh considered that an amendment was required in the package leaflet to improve clarity for patients that should tell their doctor if they have high blood pressure but also if they are being treated for high blood pressure. The wording was amended accordingly in section 2 of the Package Leaflet as set out in Annex III.

### **CMDh agreement**

The CMDh, having considered the PRAC recommendation dated 9 October 2014 pursuant to Article 107k(1) and (2) of Directive 2001/83/EC, reached an agreement on the variation of the marketing authorisations of testosterone containing medicinal products for which the relevant sections of the summary of product characteristics and package leaflet are set out in Annex III and subject to the conditions set out in Annex IV.

The timetable for the implementation of the agreement is set out in Annex V.

## **Annex III**

### **Amendments to relevant sections of the summary of product characteristics and package leaflets**

*Note:*

These amendments to the relevant sections of the Summary of Product Characteristics and package leaflet are the outcome of the referral procedure.

The product information may be subsequently updated by the Member State competent authorities, in liaison with the Reference Member State, as appropriate, in accordance with the procedures laid down in Chapter 4 of Title III of Directive 2001/83/EC.

[the wording below should be inserted in the relevant sections]

### **Summary of Product Characteristics**

#### **Section 4.1 “Therapeutic indications”**

Testosterone replacement therapy for male hypogonadism, when testosterone deficiency has been confirmed by clinical features and biochemical tests.

[...]

#### **Section 4.4 “Special Warnings and Precautions for Use”**

[...]

In patients suffering from severe cardiac, hepatic, or renal insufficiency or ischaemic heart disease, treatment with testosterone may cause severe complications characterised by oedema with or without congestive cardiac failure. In such case, treatment must be stopped immediately.

Testosterone may cause a rise in blood pressure and <name of product> should be used with caution in men with hypertension.

Testosterone level should be monitored at baseline and at regular intervals during treatment. Clinicians should adjust the dosage individually to ensure maintenance of eugonadal testosterone levels.

In patients receiving long-term androgen therapy, the following laboratory parameters should also be monitored regularly: haemoglobin, and haematocrit, liver function tests and lipid profile.

There is limited experience on the safety and efficacy of the use of <name of product> in patients over 65 years of age. Currently, there is no consensus about age specific testosterone reference values. However, it should be taken into account that physiologically testosterone serum levels are lower with increasing age.

[...]

#### **Section 4.8 Undesirable effects**

[...]

Haematocrit increased, Red blood cell count increased, Haemoglobin increased  
Frequency common.

[...]

### **Package Leaflet**

[...]

#### **1. What <name of product> is and what it is used for**

<name of product> is used in adult men for testosterone replacement to treat various health problems caused by a lack of testosterone (male hypogonadism). This should be confirmed by two separate blood testosterone measurements and also include clinical symptoms such as:

impotence

infertility

low sex drive

tiredness

depressive moods

bone loss caused by low hormone levels

[...]

## **2. What you need to know before you take <name of product>**

[...]

If you are suffering from severe heart, liver or kidney disease, treatment with <name of product> may cause severe complications in the form of water retention in your body sometimes accompanied by (congestive) heart failure.

The following blood checks should be carried out by your doctor before and during the treatment: testosterone blood level, full blood count.

Tell your doctor if you have high blood pressure or if you are treated for high blood pressure, as testosterone may cause a rise in blood pressure.

[...]

## **4. Possible side effects**

Frequency common: Increase in red blood cell count, haematocrit (percentage of red blood cells in blood) and haemoglobin (the component of red blood cells that carries oxygen), identified by periodic blood tests.

[...]

**Annex IV**  
**Conditions to the marketing authorisations**

## Conditions to the marketing authorisation

National competent authorities of Member State(s) or reference Member State(s) if applicable, shall ensure that the following conditions are fulfilled by the MAH(s):

Conditions	Date
<p>The Marketing Authorisation Holders of testosterone-containing medicinal products should, with the next PSUR:</p> <ul style="list-style-type: none"> <li>• monitor cardiovascular risk (including literature review, clinical trials data and all other relevant data) and discuss the finding in the next PSUR.</li> <li>• report on venous thrombotic events (VTE) including deep venous thrombosis (VTE) and pulmonary embolism (PE) in a separate section in the next PSUR. This section should also include literature case reports and review. The spontaneous reports shall not be presented as a listing of the individual cases, but rather as a general discussion of the aggregated cases, and include all relevant information, e.g. time to onset (when available), haematocrit/haemoglobin level (when available), indication, age, confounding factors and other.</li> <li>• discuss a possible mechanism of VTE and the potential association between CV/VTE events and testosterone levels (whether low or high levels compared to eugonadal level may contribute to the risk), and discuss if the information should be included in the product information.</li> <li>• discuss the usage in elderly, taking into account the naturally lower level of testosterone in this age group of patients. Furthermore the discussion on the adverse events in this group should be compared with the pattern of adverse events in other age groups.</li> <li>• submit the PSUR within 90 days following the DLP of 31 December 2015.</li> </ul>	<p>31 March 2016</p>



## **Annex V**

### **Timetable for the implementation of the agreement**

## Timetable for the implementation of the agreement

Adoption of CMDh agreement:	November 2014 CMDh meeting
Transmission to National Competent Authorities of the translations of the annexes to the agreement:	16 December 2014
Implementation of the agreement by the Member States (submission of the variation by the Marketing Authorisation Holder):	20 February 2015

**Appendix 1**  
**Grounds for the procedure**  
**(notification)**

**Appendix 2**  
**PRAC Recommendation**