

## 8. Malignant Disease and Immunosuppression





Contents

[8.1 Cytotoxic Drugs](#)







[8.2 Drugs affecting the immune response](#)

[8.3 Sex hormones and hormone antagonists in malignant disease](#)

**Key**

	<p><b>Red drug</b> see <a href="#">GMMMG RAG list</a>  <i>Click on the symbols to access this list</i></p>
	<p><b>Amber drug</b> see <a href="#">GMMMG RAG list</a>  <i>Click on the symbols to access this list</i></p>
	<p><b>Green drug</b> see <a href="#">GMMMG RAG list</a>  <i>Click on the symbols to access this list</i></p>
<b>U</b>	<p><b>If a medicine is unlicensed this should be highlighted in the template as follows</b>  <b>Drug name U</b></p>
	<p><b>Not Recommended</b></p>
<b>OTC</b>	<p><b>Over the Counter</b>          In line with NHS England guidance, GM do not routinely support prescribing for conditions which are self-limiting or amenable to self-care. For further details see <a href="#">GM commissioning statement</a>.</p>
<b>Order of Drug Choice</b>	<p>Where there is no preferred 1<sup>st</sup> line agent provided, the drug choice appears in alphabetical order.</p>

<b>Chapter</b>	<b>8 Malignant Disease and Immunosuppression</b>
<b>Section</b>	<b>8.1 Cytotoxic Drugs</b>
	<p>The chemotherapy of cancer is complex and should be confined to specialists in oncology and haematology. <a href="#">NPSA anti-cancer drug recommendations</a></p> <p>NOTE: a number of cytotoxic medicines that are used for indications other than cancer are listed elsewhere in this formulary under the relevant chapter e.g. methotrexate for rheumatological indications in chapter 10.</p> <p>Only trained pharmacy personnel should reconstitute cytotoxics and prescription validation should only be carried out by suitably trained pharmacists. <a href="#">Pharmacy Guidelines for the safe use of oral anti-cancer medicines</a> are available on the GMMMG website. The <a href="#">GMCCN policy and procedure for chemotherapy administration</a> provides further information.</p> <p><b>All cytotoxics with a positive NICE Health Technology Appraisal are approved for use in Greater Manchester, with a RED RAG status.</b></p> <p><a href="#">NHS England's Cancer Drug Fund</a> provides a further list of approved uses of cytotoxic drugs and the latest national funding policies.</p>
<b>Additional Notes</b>	<a href="#">Link to additional notes document</a>
<b>Subsections</b>	<b>8.1.1 Alkylating drugs, 8.1.2 Anthracyclines and other cytotoxic antibiotics, 8.1.3 Antimetabolites, 8.1.4 Vinca alkaloids and etoposide, 8.1.5 Other antineoplastic drugs</b>
<b>Additional Notes</b>	<p>All cytotoxics with a positive NICE Health Technology Appraisal are approved for use in Greater Manchester, with a RED RAG status.</p> <p><a href="#">NHS England's Cancer Drug Fund</a> provides a further list of approved uses of cytotoxic drugs and the latest national funding policies.</p> <p><b>Links to NICE guidance:</b></p> <p><a href="#">Index of NICE guidance on cancer</a></p> <p><b>Links to MHRA advice:</b></p> <p><a href="#">MHRA DSU (April 2017): Ponatinib (Iclusig▼): risk of vascular occlusive events—updated advice on possible dose reduction</a></p> <p><a href="#">MHRA DSU (May 2016): BCR-ABL tyrosine kinase inhibitors: risk of hepatitis B reactivation</a></p> <p><a href="#">MHRA DSU (May 2016): Idelalisib (Zydelig): interim measures following signal of serious infection and deaths related to infection found in clinical trials</a></p> <p><a href="#">MHRA DSU (Sept 2016): Idelalisib (Zydelig▼): updated indications and advice on minimising the risk of infection</a></p>

<b>Section</b>	<b>8.2 Drugs affecting the immune response</b>	
<b>Subsection</b>	<b>8.2.1 Antiproliferative immunosuppressant</b>	
<b>First choice</b>	<b>Azathioprine</b> Tablets 25mg, 50mg	 <a href="#">Shared care protocols available for:</a> <ul style="list-style-type: none"> <li>- IBD in adults</li> <li>- IBD in paediatrics</li> <li>- Rheumatological conditions in adults</li> <li>- Dermatology in adults</li> <li>- Neurological conditions in adults</li> <li>- Interstitial lung disease in adults</li> <li>- Autoimmune hepatitis in adults</li> </ul>
<b>Alternatives</b>	<b>Mycophenolate mofetil</b> Capsules 250mg, Tablets 500mg	 <a href="#">MHRA DSU: Mycophenolate mofetil, mycophenolic acid: new pregnancy-prevention advice for women and men 2015</a> <a href="#">NICE TA481: Immunosuppressive therapy for kidney transplant in adults</a> <a href="#">NICE TA482: Immunosuppressive therapy for kidney transplant in children and young people</a>
	<b>Mycophenolic acid</b> (Myfortic®) Gastro-resistant tablets 180mg, 360mg	
<b>Additional notes</b>		
<p>All new patients commenced on mycophenolate mofetil should be commenced on a "branded generic" preparation. Mycophenolate mofetil and mycophenolic acid are not interchangeable. Patients on Myfortic® must remain on Myfortic®.</p>		
<b>Subsection</b>	<b>8.2.2 Corticosteroids and immunosuppressants</b>	
<b>First choice</b>	<b>Ciclosporin</b> Capsules 25mg, 50mg, 100mg Oral solution 100mg/ml	 Prescribe by brand. Do not switch between brands.
<b>Alternatives</b>	<b>Tacrolimus</b> Capsules 500microgram, 1mg, 2mg, 5mg Granules 200microgram, 1mg Modified-release capsules 500microgram, 1mg, 3mg, 5mg	 <a href="#">MHRA DSU: Oral tacrolimus products: prescribe and dispense by brand name only, to minimise the risk of inadvertent switching between products, which has been associated with reports of toxicity and graft rejection, November 2017</a>
	<b>Sirolimus</b> Tablets 500microgram, 1mg, 2mg Oral solution 1mg/ml	

	<p><b>Basiliximab</b></p> <p>Powder and solvent for solution for injection 10mg, 20mg</p>	<p><b>R</b> Specialist use only</p> <p><a href="#">NICE TA481: Immunosuppressive therapy for kidney transplant in adults</a></p> <p><a href="#">NICE TA482: Immunosuppressive therapy for kidney transplant in children and young people</a></p>
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**Additional notes**

Sirolimus tablets (Rapamune®) – the 500microgram tablets are not bioequivalent with the 1mg and 2mg tablets and multiples must not be used as a substitute for the other tablet strengths.

There are 3 different oral formulations of tacrolimus:

- *Adoport®*, *Prograf®*, *Capexion®*, *Tacni®*, and *Vivadex®* are immediate-release capsules that are taken twice daily, once in the morning and once in the evening;
- *Modigraf®* granules are used to prepare an immediate-release oral suspension which is taken twice daily, once in the morning and once in the evening;
- *Advagraf®* is a prolonged-release capsule that is taken once daily in the morning.

Switching between different oral formulations of tacrolimus requires careful supervision and therapeutic monitoring by an appropriate specialist.

<b>Subsection</b>	<b>8.2.3 Antilymphocyte monoclonal antibodies</b>	
	<p><b>Alemtuzumab ▼</b></p> <p>Concentrate for IV infusion</p>	<p><b>R</b> Specialist use only</p> <p>Causes lysis of B lymphocytes</p> <p><a href="#">NICE TA312: Alemtuzumab for treating relapsing-remitting multiple sclerosis</a></p>
	<p><b>Natalizumab ▼</b></p> <p>Concentrate for solution for infusion 300mg/15ml</p>	<p><b>R</b> Specialist use only</p> <p><a href="#">MHRA DSU: Natalizumab (Tysabri): progressive multifocal leukoencephalopathy – updated advice to support early detection (April 2016)</a></p> <p><a href="#">NICE TA127: Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis</a></p>
	<p><b>Ocrelizumab ▼</b></p> <p>Concentrate for solution for infusion 300mg/10ml</p>	<p><b>R</b> Specialist use only</p> <p><a href="#">NICE TA533: Ocrelizumab for treating relapsing-remitting multiple sclerosis</a></p>
	<p><b>Ofatumumab ▼</b></p> <p>20 mg solution for injection in pre-filled pen</p>	<p><b>R</b> Specialist use only</p> <p><a href="#">NICE TA699: Ofatumumab for treating relapsing multiple sclerosis</a></p>


Subsection	8.2.4 Other immune-modulating drugs	
<b>Interferon Alfa</b>		
	<p><b>Interferon alfa-2b (rbe)</b> IntronA® Solution for injection (for subcutaneous injection or intravenous infusion) Solution for injection pen (for SC injection)</p> <p><b>Interferon alfa-2a (rbe)</b> Roferon-A® Solution for injection pre-filled syringes (for subcutaneous use) Solution for injection cartridges (for <i>Roferon</i>® pen device, subcutaneous and intramuscular use) Solution for injection vials (for subcutaneous and intramuscular use)</p>	<p><b>R</b></p> <p><b>R</b></p>
<b>Peginterferon Alfa</b>		
	<p><b>Peginterferon alfa-2a (rbe)</b> Pegasys® Solution for injection pre-filled syringe (for subcutaneous injection)</p> <p><b>Peginterferon alfa-2b (rbe)</b> ViraferonPeg® Powder and solvent for solution for injection pre-filled pen (for subcutaneous injection)</p>	<p><b>R</b></p> <p><b>R</b></p> <p><a href="#">NICE TA75: peginterferon alfa, interferon alfa, and ribavirin for chronic hepatitis C</a></p> <p><a href="#">NICE TA300: peginterferon alfa and ribavirin for treating chronic hepatitis C in children and young people</a></p>
<b>Interferon Beta</b>		
	<p><b>Interferon beta-1a</b> Avonex®, Rebif® Solution for injection pre-filled syringe Solution for injection pre-filled pens Powder and solvent for solution for injection vials Solution for injection cartridges (for RebiSmart® device)</p>	<p><b>R</b></p> <p><a href="#">NICE TA527: Beta interferons and glatiramer acetate for treating multiple sclerosis</a></p> <p><a href="#">MHRA DSU: Interferon beta: risk of thrombotic microangiopathy and risk of nephrotic syndrome, Oct 2014</a></p>
	<p><b>Interferon beta-1b</b> Betaferon® Powder and solvent for solution for injection</p>	<p><b>R</b></p> <p><a href="#">NICE TA527: Beta interferons and glatiramer acetate for treating multiple sclerosis</a></p> <p><a href="#">MHRA DSU: Interferon beta: risk of thrombotic microangiopathy and risk of nephrotic syndrome, Oct 2014</a></p>
<b>Peginterferon beta</b>		
	<p><b>Peginterferon beta-1a</b> Plegridy® Solution for injection pre-filled pen (for subcutaneous injection)</p>	<p><b>R</b></p> <p><a href="#">NICE TA624: Peginterferon beta-1a for treating relapsing-remitting multiple sclerosis</a></p>

**Additional notes**

See also NHS England [Specialised Commissioning policies for Neurosciences](#), including Treatment Algorithm for Multiple Sclerosis Disease-Modifying Therapies.

	<p><b>Canakinumab ▼</b> Powder for solution for injection vial 150mg</p>	<p><b>R</b> Specialist use only</p>
	<p><b>Cladribine</b> Mavenclad® Tablets 10mg</p>	<p><b>R</b> <a href="#">NICE TA616</a>: Cladribine for treating relapsing-remitting multiple sclerosis</p>
	<p><b>Dimethyl fumarate</b> Capsules 120mg and 240mg</p>	<p><b>R</b> Specialist use only</p> <p><a href="#">NICE TA320: Dimethyl fumarate for treating relapsing-remitting MS</a></p> <p><a href="#">MHRA DSU: Dimethyl fumarate (Tecfidera®): fatal PML in an MS patient with severe prolonged lymphopenia, March 2015</a></p> <p><a href="#">MHRA DSU: Dimethyl fumarate (Tecfidera): updated advice on risk of progressive multifocal leukoencephalopathy (April 2016)</a></p> <p><a href="#">MHRA DSU: Dimethyl fumarate (Tecfidera): updated advice on the risk of progressive multifocal leukoencephalopathy (PML) associated with mild lymphopenia, Jan 2021</a></p>
	<p><b>Fingolimod ▼</b> Capsules 500microgram</p>	<p><b>R</b></p> <p>MHRA DSUs:</p> <ul style="list-style-type: none"> <li>• <a href="#">Fingolimod (Gilenya ▼): updated advice about the risks of serious liver injury and herpes meningoencephalitis, Jan 2021</a></li> <li>• <a href="#">Fingolimod (Gilenya ▼): increased risk of congenital malformations; new contraindication during pregnancy and in women of childbearing potential not using effective contraception, Sept 2019</a></li> <li>• <a href="#">Fingolimod (Gilenya ▼): updated advice about risk of cancers and serious infections, Dec 2017</a></li> <li>• <a href="#">Fingolimod (Gilenya ▼) new contraindications for patients with pre-existing cardiac disorders, Dec 2017</a></li> <li>• <a href="#">MS therapies: signal of rebound effect after stopping or switching therapy, April 2017</a></li> <li>• <a href="#">Fingolimod (Gilenya ▼): risks of progressive multifocal leukoencephalopathy, basal-cell carcinoma, and opportunistic infections (April 2016)</a></li> <li>• <a href="#">Bradycardia and heart block, Jan 2013</a></li> <li>• <a href="#">Fingolimod: not recommended for patients at known risk for cardiovascular adverse events, May 2012</a></li> </ul> <p><a href="#">NICE TA254: Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis</a></p>

	<p><b>Glatiramer acetate</b> Copaxone® Solution for injection pre-filled syringe 20mg/ml</p>	<p><b>R</b> <a href="#">NICE TA527: Beta interferons and glatiramer acetate for treating multiple sclerosis</a></p>
	<p><b>Siponimod</b> Tables 0.25 mg and 2 mg</p>	<p>RAG status pending <a href="#">NICE TA656: Siponimod for treating secondary progressive multiple sclerosis</a></p>
<p><b>Additional notes</b> See also NHS England <a href="#">Specialised Commissioning policies for Neurosciences</a>, including Treatment Algorithm for Multiple Sclerosis Disease-Modifying Therapies.</p>		

<b>Section</b>	<b>8.3 Sex hormones and hormone antagonists in malignant disease</b>	
<b>Subsection</b>	<b>8.3.1 Oestrogens</b>	
	<b>Diethylstilbestrol</b> Tablets 1mg, 5mg <b>Ethinylestradiol</b> Tablets 10microgram, 50microgram, 1mg	G <sub>n</sub> following specialist initiation
<b>Subsection</b>	<b>8.3.2 Progestogens</b>	
	<b>Medroxyprogesterone acetate</b> Tablets 10mg, 100mg, 200mg <b>Megestrol acetate</b> Tablets 160mg	G <sub>n</sub> following specialist initiation
<b>Subsection</b>	<b>8.3.4 Hormone antagonists</b>	
<b>Subsection</b>	<b>8.3.4.1 Breast cancer</b>	
	<b>Anastrozole</b> Tablets 1mg	G <sub>n</sub> following specialist advice
	<b>Exemestane</b> Tablets 25mg	G <sub>n</sub> following specialist advice
	<b>Letrozole</b> Tablets 2.5mg	G <sub>n</sub> following specialist advice
	<b>Tamoxifen</b> Tablets 10mg, 20mg	G <sub>n</sub> following specialist advice
<b>Do Not Prescribe</b>	<b>Fulvestrant</b> Solution for injection (Faslodex®)	Criterion 2 (see RAG list)
<b>Additional notes</b>		
<a href="#">Link to additional notes document</a> <a href="#">NICE TA112 Breast cancer (early) - hormonal treatments</a>		
<b>Subsection</b>	<b>8.3.4.2 Gonadorelin analogues and gonadotrophin-releasing hormone antagonists</b>	
<b>Gonadorelin analogues</b>		
	<b>Goserelin</b> Zoladex® Implant pre-filled syringe 3.6mg (four weeks) Implant pre-filled syringe 10.8mg (twelve weeks)	 (for licensed indications) <a href="#">GMMMG SCPs:</a> <ul style="list-style-type: none"> <li>Goserelin in breast cancer</li> <li>Goserelin (Zoladex), Leuprorelin (Prostap) or Triptorelin (Decapeptyl SR) in the treatment of prostate cancer in Adults</li> </ul>



		<ul style="list-style-type: none"> <li>GnRH analogues for patients aged 17 years or over under Indigo Gender Service</li> </ul>
	<p><b>Leuprorelin</b> Prostav®</p> <p>Suspension for injection pre-filled syringe 3.75mg (four weeks)</p> <p>Suspension for injection pre-filled syringe 11.25mg (three months)</p>	<p><b>A</b> (for licensed indications)</p> <p><a href="#">GMMMG SCP: Goserelin (Zoladex), Leuprorelin (Prostav) or Triptorelin (Decapeptyl SR) in the treatment of prostate cancer in Adults</a></p> <p><a href="#">GMMMG SCP: GnRH analogues for patients aged 17 years or over under Indigo Gender Service</a></p>
	<p><b>Triptorelin</b> Decapeptyl®</p> <p>Suspension for injection vials 3mg (every four weeks)</p> <p>Suspension for injection vials 11.25mg (every three months)</p> <p>Suspension for injection vials 22.5mg (every six months)</p> <p><b>Triptorelin</b> Gonapeptyl®</p> <p>Suspension for injection pre-filled devices 3.75mg (every four weeks)</p>	<p><b>A</b> (for licensed indications)</p> <p><a href="#">GMMMG SCP: Goserelin (Zoladex), Leuprorelin (Prostav) or Triptorelin (Decapeptyl SR) in the treatment of prostate cancer in Adults</a></p> <p><a href="#">GMMMG SCP: GnRH analogues for patients aged 17 years or over under Indigo Gender Service</a></p>
<b>Anti-androgens</b>		
	<p><b>Bicalutamide</b></p> <p>Tablets 50mg, 150mg</p> <p><b>Cyproterone acetate</b></p> <p>Tablets 50mg, 100mg</p>	<p><b>G<sub>n</sub></b> following specialist initiation.</p> <p>NB: unlicensed if used in prostate cancer (metastatic) with the aim of retaining sexual function</p> <p><b>G<sub>n</sub></b> following specialist initiation</p>
<b>Gonadotrophin-releasing hormone antagonists</b>		
	<p><b>Degarelix</b></p> <p>Powder for solution for injection 80mg, 120mg</p>	<p><b>A</b></p> <p><a href="#">TA404: Degarelix for treating advanced hormone-dependent prostate cancer</a></p> <p><a href="#">GMMMG SCP: Degarelix in advanced hormone dependent prostate cancer</a></p>
<p><b>Additional notes</b> <a href="#">Link to additional notes document</a></p>		
<b>Subsection</b>	<b>8.3.4.3 Somatostatin analogues</b>	
<b>First choice</b>	<p><b>Octreotide</b></p>	<p><b>R</b></p> <p><a href="#">See HCD commissioning statement</a></p>

	<p>Solution for injection (various forms)            50microgram/1ml 100microgram/1ml,            500microgram/1ml, 1mg/5ml</p> <p>Suspension for injection (depot) 10mg, 20mg, 30mg</p>	
<b>Alternatives</b>	<p><b>Lanreotide</b></p> <p>Solution for injection pre-filled syringe 60mg, 90mg,            120mg</p>	<b>R</b>
<p><b>Additional notes</b> <a href="#">Link to additional notes document</a></p>		