8. Malignant Disease and Immunosuppression

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8.1 Cytotoxic Drugs
8.2 Drugs affecting the immune response
8.3 Sex hormones and hormone antagonists in malignant disease

For cost information please go to the most recent cost comparison charts

Key

<table>
<thead>
<tr>
<th></th>
<th>Red drug see GMMMG RAG list</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Amber drug see GMMMG RAG list</td>
</tr>
<tr>
<td>G</td>
<td>Green drug see GMMMG RAG list</td>
</tr>
<tr>
<td>U</td>
<td>If a medicine is unlicensed this should be highlighted in the template as follows: Drug name U</td>
</tr>
<tr>
<td></td>
<td>Not Recommended</td>
</tr>
<tr>
<td>OTC</td>
<td>Over the Counter</td>
</tr>
</tbody>
</table>

Order of Drug Choice Where there is no preferred 1st line agent provided, the drug choice appears in alphabetical order.
Chapter 8 Malignant Disease and Immunosuppression

Section 8.1 Cytotoxic Drugs

The chemotherapy of cancer is complex and should be confined to specialists in oncology and haematology. NPSA anti-cancer drug recommendations

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.

Only trained pharmacy personnel should reconstitute cytotoxics and prescription validation should only be carried out by suitably trained pharmacists. Pharmacy Guidelines for the safe use of oral anti-cancer medicines are available on the GMMMG website. The GMCCN policy and procedure for chemotherapy administration provides further information.

All cytotoxics with a positive NICE Health Technology Appraisal are approved for use in Greater Manchester.

NHS England’s Cancer Drug Fund provides a further list of approved uses of cytotoxic drugs and the latest national funding policies.

Treatment for cytotoxic-induced side effects

Mucositis and myelosuppression

**Calcium Folinate**
Tablets 15mg

**Folinic acid** (as calcium salt)
Solution for injection 100mg/2ml, 400mg/8ml and 900mg/18ml

**Levofolinic acid** (as calcium salt)
Solution for injection 25mg/2.5ml, 175mg/17.5ml

Urothelial toxicity

**Mesna**
Tablets: 400mg, 600mg
Solution for injection 400mg/4ml, 1g/10ml

Additional Notes Link to additional notes document

Subsections 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
Additional Notes

All cytotoxics with a positive NICE Health Technology Appraisal are approved for use in Greater Manchester. 
[NHS England’s Cancer Drug Fund](#) provides a further list of approved uses of cytotoxic drugs and the latest national funding policies.

Links to NICE guidance:

NICE CG131: Colorectal cancer
NG52: Non-Hodgkin’s lymphoma: diagnosis and management

Links to MHRA advice:

MHRA DSU (April 2017): Ponatinib (Iclusig▼): risk of vascular occlusive events—updated advice on possible dose reduction
MHRA DSU (May 2016): BCR-ABL tyrosine kinase inhibitors: risk of hepatitis B reactivation
MHRA DSU (May 2016): Idelalisib (Zydelig): interim measures following signal of serious infection and deaths related to infection found in clinical trials
MHRA DSU (Sept 2016): Idelalisib (Zydelig▼): updated indications and advice on minimising the risk of infection
## Section 8.2  Drugs affecting the immune response

### Subsection 8.2.1  Antiproliferative immunosuppressant

| First choice | **Azathioprine**  
Tablets 25mg, 50mg |
|-------------|------------------|
| Alternatives | **Mycophenolate Mofetil**  
Capsules 250mg, Tablets 500mg |
| | **Mycophenolic acid** *(Myfortic®)*  
Gastro-resistant tablets 180mg, 360mg |

**GM SCG: Azathioprine for Interstitial Lung Disease**

**MHRA DSU: Mycophenolate mofetil, mycophenolic acid: new pregnancy-prevention advice for women and men 2015**

**NICE TA85: Renal transplantation - immuno-suppressive regimens (adults)**

**NICE TA99: Renal transplantation - immunosuppressive regimens (adolescents)**

### Additional notes

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®.

### Subsection 8.2.2  Corticosteroids and immunosuppressant

| First choice | **Ciclosporin**  
Capsules 25mg, 50mg, 100mg  
Oral solution 100mg/ml |
|-------------|------------------|
| Alternatives | **Tacrolimus**  
Capsules 500microgram, 1mg, 2mg, 5mg  
Granules 200microgram, 1mg  
Modified-release capsules 500microgram, 1mg, 3mg, 5mg |
| | **Sirolimus**  
Tablets 500microgram, 1mg, 2mg  
Oral solution 1mg/ml |
| | **Basiliximab**  
Powder and solvent for solution for injection 10mg, 20mg |

**Prescribe by brand. Do not switch between brands.**

**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, June 2012**

**Specialist use only**

**NICE TA85 – Immunosuppressive therapy for renal transplantation in adults**
### 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.

### Subsection 8.2.3 Antilymphocyte monoclonal antibodies

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Formulation</th>
<th>Use</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alemtuzumab</strong></td>
<td>Concentrate for IV infusion</td>
<td>Specialist use only</td>
<td>Causes lysis of B lymphocytes</td>
</tr>
<tr>
<td><strong>Blinatumomab</strong></td>
<td>38.5 micrograms powder for concentrate and solution for infusion.</td>
<td>Specialist use only</td>
<td>Causes lysis of B lymphocytes</td>
</tr>
<tr>
<td><strong>Daclizumab</strong></td>
<td>150mg solution for injection in pre-filled syringe/pen for subcutaneous injection</td>
<td>Specialist use only</td>
<td>Causes lysis of B lymphocytes</td>
</tr>
<tr>
<td><strong>Ofatumumab</strong></td>
<td>Concentrate for IV infusion</td>
<td>Specialist use only</td>
<td>Causes lysis of B lymphocytes</td>
</tr>
<tr>
<td><strong>Obinutuzumab</strong></td>
<td>Concentrate for IV infusion</td>
<td>Specialist use only</td>
<td>Causes lysis of B lymphocytes</td>
</tr>
<tr>
<td><strong>Rituximab</strong></td>
<td>Concentrate for IV infusion</td>
<td>Specialist use only</td>
<td><strong>NICE TA243</strong>: Rituximab for the first-line treatment of stage III-IV follicular lymphoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>NICE TA226</strong>: Rituximab for the first-line maintenance treatment of follicular non-Hodgkin’s lymphoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><strong>NICE TA65</strong>: Rituximab for aggressive non-Hodgkin’s</td>
</tr>
</tbody>
</table>
### 8.2.4 Other immunomodulating drugs

#### Interferon Alfa

**Interferon alfa-2b (rbe) IntronA®**
- Solution for injection (for subcutaneous injection or intravenous infusion)
- Solution for injection pen (for SC injection)

**Interferon alfa-2a (rbe) Roferon-A®**
- Solution for injection pre-filled syringes (for subcutaneous use)
- Solution for injection cartridges (for Roferon® pen device, subcutaneous and intramuscular use)
- Solution for injection vials (for subcutaneous and intramuscular use)

#### PegInterferon Alfa

**Peginterferon alfa-2a (rbe) Pegasys®**
- Solution for injection pre-filled syringe (for subcutaneous injection)

**Peginterferon alfa-2b (rbe) ViraferonPeg®**
- Powder and solvent for solution for injection pre-filled pen (for subcutaneous injection)

#### Additional notes

**Interferon Beta**

**Interferon beta–1a 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)

**Interferon beta–1b Betaferon®**
- Powder and solvent for solution for injection

**Additional notes**

NICE produced guidance (NICE TA32) on the use of beta interferon and glatiramer acetate which did not recommend them, because although it states that they work, there remains uncertainty about which patients benefit from these medicines and to what extent. The Department of Health (DH) produced a risk sharing scheme recommending these treatments, and helping ensure that they be made cost effective for the NHS to commission. (DH Health Service Circular HSC 2002/004). These treatments are now covered by NHS England policy Disease Modifying Therapies for Patients with Multiple Sclerosis (Ref: NHSCB/D04/P/a).

### BCG bladder instillation

<table>
<thead>
<tr>
<th></th>
<th></th>
<th>Specialist use only</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Connaught strain BCG</strong></td>
<td>ImmuCyst®</td>
<td>Bladder instillation vials 81mg</td>
</tr>
<tr>
<td><strong>TICE strain BCG</strong></td>
<td>OncoTICE®</td>
<td>Bladder instillation vial 12.5mg</td>
</tr>
</tbody>
</table>

**Additional notes**  [Link to additional notes document](#)

### Canakinumab

<table>
<thead>
<tr>
<th>Canakinumab ▼</th>
<th>Powder for solution for injection vial 150mg</th>
<th>Specialist use only</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimethyl fumarate</td>
<td>Capsules 120mg and 240mg</td>
<td>Specialist use only</td>
</tr>
</tbody>
</table>

**Additional notes**  [Link to additional notes document](#)

- NICE TA320: Dimethyl fumarate for treating relapsing-remitting MS
- MHRA DSU: Dimethyl fumarate (Tecfidera®): fatal PML in an MS patient with severe prolonged lymphopenia
- Patient with severe, prolonged lymphopenia, March 2015
- MHRA DSU: Dimethyl fumarate (Tecfidera®): updated advice on risk of progressive multifocal leukoencephalopathy (April 2016)
**Fingolimod**

- **Fingolimod ▼**
  - Capsules 500microgram

  **MHRA DSU:** MS therapies: signal of rebound effect after stopping or switching therapy
  **MHRA DSU:** Fingolimod (Gilenya): risks of progressive multifocal leukoencephalopathy, basal-cell carcinoma, and opportunistic infections (April 2016)
  **MHRA DSU:** fingolimod: not recommended for patients at known risk for cardiovascular adverse events, May 2012
  **MHRA DSU:** bradycardia and heart block, Jan 2013
  **NICE TA254:** Fingolimod for the treatment of highly active relapsing-remitting multiple sclerosis

**Additional notes** [Link to additional notes document](#)

**Glatiramer acetate**

- **Glatiramer acetate** Copaxone®
  - Solution for injection pre-filled syringe 20mg/ml

**Additional notes**

NICE produced guidance [NICE TA32](#) for the use of beta interferon and glatiramer acetate which did not recommend them, because although it states that they work, there remains uncertainty about which patients benefit from these medicines and to what extent. The Department of Health (DH) produced a risk sharing scheme recommending these treatments, and helping ensure that they be made cost effective for the NHS to commission. ([DH Health Service Circular HSC 2002/004](#)). These treatments are now covered by NHS England policy Disease Modifying Therapies for Patients with Multiple Sclerosis (Ref: NHSCB/D04/P/a).

**Lenalidomide and thalidomide**

- **Thalidomide**
  - Capsules 50mg

  **MHRA DSU:** Thalidomide: reduced starting dose in patients older than age 75 years. 2015
  **NICE TA228:** bortezomib and thalidomide for the first-line treatment of multiple myeloma

- **Lenalidomide**
  - Capsules 5mg, 10mg, 15mg, 25mg

  **NICE TA171:** lenalidomide for the treatment of multiple myeloma
  **NICE TA322:** Lenalidomide for treating myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality
<table>
<thead>
<tr>
<th>Additional notes</th>
<th>Link to additional notes document</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE NG35: Myeloma diagnosis and management</td>
<td></td>
</tr>
<tr>
<td>NICE TA338: Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib – NOT RECOMMENDED</td>
<td></td>
</tr>
<tr>
<td>MHRA DSU (May 2016): Pomalidomide (Imnovid): risk of hepatitis B reactivation</td>
<td></td>
</tr>
<tr>
<td>MHRA DSU (May 2015): Pomalidomide (Imnovid): risks of cardiac failure, interstitial lung disease and hepatotoxicity</td>
<td></td>
</tr>
</tbody>
</table>
### Mifamurtide

**Mifamurtide** (mifamurtide encapsulated in liposomes)
Powder for suspension for infusion vials 4mg (for intravenous use)

| Specialist use only | NICE TA235: Mifamurtide for the treatment of osteosarcoma |

### Additional notes
[Link to additional notes document](#)

### Natalizumab

**Natalizumab ▼**
Concentrate for solution for infusion 300mg/15ml

| Specialist use only | MHRA DSU: Natalizumab (Tysabri): progressive multifocal leukoencephalopathy – updated advice to support early detection (April 2016) NICE TA127: Natalizumab for the treatment of adults with highly active relapsing-remitting multiple sclerosis |

### Pegaspargase

**Pegaspargase▼**
(The active substance is a covalent conjugate of \( L-asparaginase \) with \( \text{monomethoxypropylene glycol} \))
Solution for injection/infusion 750 U/ml

| Specialist use only | (Awaiting RAG classification) |
### Section 8.3  Sex hormones and hormone antagonists in malignant disease

#### Subsection 8.3.1 Oestrogens

<table>
<thead>
<tr>
<th><strong>Diethylstilbestrol</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets 1mg, 5mg</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Ethinylestradiol</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets 10microgram, 50microgram, 1mg</td>
</tr>
</tbody>
</table>

#### Subsection 8.3.2 Progestogens

<table>
<thead>
<tr>
<th><strong>Medroxyprogesterone acetate</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets 10mg, 100mg, 200mg</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Megestrol acetate</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets 160mg</td>
</tr>
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</table>

#### Subsection 8.3.4 Hormone antagonists

##### Subsection 8.3.4.1 Breast cancer

<table>
<thead>
<tr>
<th><strong>Anastrozole</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets 1mg</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Exemestane</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets 25mg</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Letrozole</strong></th>
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</thead>
<tbody>
<tr>
<td>Tablets 2.5mg</td>
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</table>

<table>
<thead>
<tr>
<th><strong>Tamoxifen</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Tablets 10mg, 20mg</td>
</tr>
</tbody>
</table>

Additional notes

[Link to additional notes document](#)

NICE TA112 Breast cancer (early) - hormonal treatments

#### Subsection 8.3.4.2 Gonadorelin analogues and gonadotrophin-releasing hormone antagonists

**Gonadorelin analogues**

<table>
<thead>
<tr>
<th><strong>Goserelin</strong> Zoladex®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implant pre-filled syringe 3.6mg (four weeks)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Leuprolelin</strong> Prostap®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspension for injection pre-filled syringe 3.75mg (four weeks)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Triptorelin</strong> Decapeptyl® Gonapeptyl®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspension for injection pre-filled devices 3.75mg (every four weeks)</td>
</tr>
</tbody>
</table>

(for licensed indications)

GMMMG SCP: GOSERELIN in breast cancer

(for licensed indications)

GMMMG SCP: LEUPROLELIN in prostate cancer

(for licensed indications)

GMMMG SCP: TRIPTORELIN in prostate cancer

Locally advanced non-metastatic tamocancer as alternative to surgical castration, metastatic prostate cancer, as an adjuvant to radiotherapy in high risk localised or locally advanced prostate cancer by intramuscular injection
## Anti-androgens

<p>| | |</p>
<table>
<thead>
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</thead>
<tbody>
<tr>
<td><strong>Bicalutamide</strong></td>
<td>Tablets 50mg, 150mg</td>
</tr>
<tr>
<td><strong>Cyproterone acetate</strong></td>
<td>Tablets 50mg, 100mg</td>
</tr>
<tr>
<td><strong>Enzalutamide</strong></td>
<td>Capsules 40mg</td>
</tr>
</tbody>
</table>

NICE TA316: Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regime

## Gonadotrophin-releasing hormone antagonists

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<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Degarelix</strong></td>
<td>Powder for solution for injection 80mg, 120mg</td>
</tr>
</tbody>
</table>

TA404: Degarelix for treating advanced hormone-dependent prostate cancer

GMMMG SCP: Degarelix in advanced hormone dependent prostate cancer

## Subsection 8.3.4.3 Somatostatin analogues

### First choice

<p>| | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Octreotide</strong></td>
<td>Solution for injection (various forms) 50microgram/1ml 100microgram/1ml, 500microgram/1ml, 1mg/5ml</td>
</tr>
<tr>
<td></td>
<td>Suspension for injection (depot) 10mg, 20mg, 30mg</td>
</tr>
</tbody>
</table>

(for licensed indications)

### Alternatives

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>Lanreotide</strong></td>
<td>Solution for injection pre-filled syringe 60mg, 90mg, 120mg</td>
</tr>
</tbody>
</table>

(for licensed indications)

Additional notes [Link to additional notes document](#)