8. Malignant Disease and Immunosuppression

Contents

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

Key

R	**Red drug** see GMMMG RAG list
A	**Amber drug** see GMMMG RAG list
Gn	**Green drug** see GMMMG RAG list
U	If a medicine is unlicensed this should be highlighted in the template as follows: **Drug name** U
	Not Recommended
OTC	**Over the Counter**
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:

Index of NICE guidance on cancer

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	A GM SCG: Azathioprine for Interstitial Lung Disease
Alternatives	**Mycophenolate Mofetil** Capsules 250mg, Tablets 500mg	A MHRA DSU: Mycophenolate mofetil, mycophenolic acid: new pregnancy-prevention advice for women and men 2015 NICE TA481: Immunosuppressive therapy for kidney transplant in adults NICE TA482: Immunosuppressive therapy for kidney transplant in children and young people
	Mycophenolic acid (Myfortic®) Gastro-resistant tablets 180mg, 360mg	A
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	A Prescribe by brand. Do not switch between brands.
Alternatives	**Tacrolimus** Capsules 500microgram, 1mg, 2mg, 5mg Granules 200microgram, 1mg Modified-release capsules 500microgram, 1mg, 3mg, 5mg	A 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
	Sirolimus Tablets 500microgram, 1mg, 2mg Oral solution 1mg/ml	A
	Basiliximab Powder and solvent for solution for injection 10mg, 20mg	R Specialist use only NICE TA481: Immunosuppressive therapy for kidney transplant in adults NICE TA482: Immunosuppressive therapy for kidney transplant in children and young people

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	
	Alemtuzumab ▼ Concentrate for IV infusion	(R) Specialist use only Causes lysis of B lymphocytes NICE TA312: Alemtuzumab for treating relapsing-remitting multiple sclerosis
	Blinatumomab▼ 38.5 micrograms powder for concentrate and solution for infusion.	(R) Specialist use only NICE TA450: Blinatumomab for previously treated Philadelphia-chromosome-negative acute lymphoblastic leukaemia
	Daclizumab▼ 150mg solution for injection in pre-filled syringe/pen for subcutaneous injection	(R) Specialist use only NICE TA441: Daclizumab for treating relapsing-remitting MS
	Ofatumumab ▼ Concentrate for IV infusion	(R) Specialist use only **Causes lysis of B lymphocytes** NICE TA344: Ofatumumab in combination with chlorambucil or bendamustine for untreated chronic lymphocytic leukaemia MHRA DSU: Ofatumumab - screen for hepatitis B virus before treatment, Jan 2014 MHRA DSU: Ofatumumab - reminder of risk of serious and fatal infusion reactions—always give premedication and monitor patients carefully, Aug 2014
	Obinutuzumab ▼ Concentrate for IV infusion	(R) Specialist use only NICE TA343: Obinutuzumab in combination with chlorambucil for untreated chronic lymphocytic leukaemia
	Rituximab▼ Concentrate for IV infusion	(R) Specialist use only NICE TA243: Rituximab for the first-line treatment of stage III-IV follicular lymphoma NICE TA137: Rituximab for the treatment of relapsed or refractory stage III or IV follicular non-Hodgkin's lymphoma NICE TA226: Rituximab for the first-line maintenance treatment of follicular non-Hodgkin's lymphoma NICE TA174: Rituximab for the first-line treatment of chronic lymphocytic leukaemia NICE TA65: Rituximab for aggressive non-Hodgkin's

		lymphoma NICE TA308: Vasculitis (anti-neutrophil cytoplasmic antibody-associated) – rituximab (with glucocorticoids)
Subsection	**8.2.4 Other immunomodulating drugs**	
Interferon Alfa		
Alternatives	**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)	R R
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)	R R NICE TA75: peginterferon alfa, interferon alfa, and ribavirin for chronic hepatitis C NICE TA300: peginterferon alfa and ribavirin for treating chronic hepatitis C in children and young people
Additional notes **Link to additional notes document**		
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)	R
	Interferon beta–1b Betaferon® Powder and solvent for solution for injection	R
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). MHRA DSU: Interferon beta: risk of thrombotic microangiopathy and risk of nephrotic syndrome, Oct 2014		

BCG bladder instillation		
	Connaught strain BCG ImmuCyst® Bladder instillation vials 81mg **TICE strain BCG** OncoTICE® Bladder instillation vial 12.5mg	Specialist use only Specialist use only
Additional notes Link to additional notes document		
Canakinumab		
	Canakinumab ▼ Powder for solution for injection vial 150mg **Dimethyl fumarate** Capsules 120mg and 240mg	Specialist use only Ⓡ Specialist use only 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)
Additional notes Link to additional notes document		

Cladribine		
	Cladribine Mavenclad® Tablets 10mg	Ⓡ NICE TA493: Cladribine tablets for relapsing-remitting multiple sclerosis
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 (Gilenya▼): updated advice about risk of cancers and serious infections, Dec 2017 MHRA DSU: Fingolimod: not recommended for patients at known risk for cardiovascular adverse events, May 2012 MHRA DSU: bradycardia and heart block, Jan 2013 MHRA DSU: Fingolimod (Gilenya▼) new contraindications for patients with pre-existing cardiac disorders, Dec 2017 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	(R) 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	(R) NICE TA171: lenalidomide for the treatment of multiple myeloma NICE TA322: Lenalidomide for treating myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality

Additional notes Link to additional notes document

NICE NG35: Myeloma diagnosis and management
NICE TA338: Pomalidomide for relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib – NOT RECOMMENDED
MHRA DSU (May 2016): Pomalidomide (Imnovid): risk of hepatitis B reactivation
MHRA DSU (May 2015): Pomalidomide (Imnovid): risks of cardiac failure, interstitial lung disease and hepatotoxicity

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 Escherichia coli-derived L-asparaginase with 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**	
	Diethylstilbestrol Tablets 1mg, 5mg **Ethinylestradiol** Tablets 10microgram, 50microgram, 1mg	
Subsection	**8.3.2 Progestogens**	
	Medroxyprogesterone acetate Tablets 10mg, 100mg, 200mg **Megestrol acetate** Tablets 160mg	
Subsection	**8.3.4 Hormone antagonists**	
Subsection	**8.3.4.1 Breast cancer**	
	Anastrozole Tablets 1mg	Gn following specialist initiation
	Exemestane Tablets 25mg	Gn following specialist initiation
	Letrozole Tablets 2.5mg	Gn following specialist initiation
	Tamoxifen Tablets 10mg, 20mg	Gn following specialist initiation
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		
	Goserelin Zoladex® Implant pre-filled syringe 3.6mg (four weeks) Implant pre-filled syringe 10.8mg (twelve weeks) **Leuprorelin** Prostap® Suspension for injection pre-filled syringe 3.75mg (four weeks) Suspension for injection pre-filled syringe 11.25mg (three months) **Triptorelin** Decapeptyl®, Gonapeptyl® Suspension for injection pre-filled devices 3.75mg (every four weeks) Suspension for injection vials 3mg (every four weeks) Suspension for injection vials 11.25mg (every three months) Suspension for injection vials 22.5mg (every six months)	A (for licensed indications) GMMMG SCP: GOSERELIN in breast cancer A (for licensed indications) A (for licensed indications) 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		
	Bicalutamide Tablets 50mg, 150mg **Cyproterone acetate** Tablets 50mg, 100mg **Enzalutamide** ▼ Capsules 40mg	Gn following specialist initiation NICE TA316: Enzalutamide for metastatic hormone-relapsed prostate cancer previously treated with a docetaxel-containing regime
Gonadotrophin-releasing hormone antagonists		
	Degarelix Powder for solution for injection 80mg, 120mg	R TA404: Degarelix for treating advanced hormone-dependent prostate cancer GMMMG SCP: Degarelix in advanced hormone dependent prostate cancer
Additional notes Link to additional notes document		
Subsection	**8.3.4.3 Somatostatin analogues**	
First choice	**Octreotide** Solution for injection (various forms) 50microgram/1ml 100microgram/1ml, 500microgram/1ml, 1mg/5ml Suspension for injection (depot) 10mg, 20mg, 30mg	A (for licensed indications) R other indications
Alternatives	**Lanreotide** Solution for injection pre-filled syringe 60mg, 90mg, 120mg	A (for licensed indications) R other indications
Additional notes Link to additional notes document		