Mogamulizumab Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
As monotherapy for the treatment of adult patients with mycosis fungoides (MF) or Sézary syndrome (SS) who have received at least one prior systemic therapy.	C84	00761a	ODMS 01/05/2023

* This is for post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Treatment is administered weekly on days 1, 8, 15 and 22 of the first 28-day cycle, followed by administration every two weeks on Days 1 and 15 of each subsequent 28-day cycle until disease progression or unacceptable toxicity.

Facilities to treat anaphylaxis MUST be present when systemic anti-cancer therapy (SACT) is administered.

Day	Drug	Dose	Route	Diluent & Rate	Cycle
1, 8, 15, 22	Mogamulizumab[a]	1mg/kg	IV infusion	250mL[b] NaCl 0.9% over 60 minutes[c]	Cycle 1 only
1, 15	Mogamulizumab[a]	1mg/kg	IV infusion	250mL[b] NaCl 0.9% over 60 minutes[c]	Cycle 2 onwards
[a]Administration should occur within 2 days of the scheduled day. If a dose is missed by more than 2 days, the next dose should be administered as soon as possible, after which the dosing schedule should be resumed with doses given based on the new scheduled days.					
[b]Mogamulizumab is diluted to a final concentration ranging from 0.1mg/mL to 3.0mg/mL.					
[c]Administer infusion solution through an intravenous line containing a sterile, low protein binding 0.22 micron (or equivalent) in-line filter.					

Note: Administration volumes and fluids have been standardised to facilitate electronic prescribing system builds.

ELIGIBILITY:

- Indication as above
- ECOG 0-1
- Age ≥ 18 years
- At least one prior systemic therapy
- Adequate haematological, hepatic and renal function
- Histologically confirmed diagnosis of mycosis fungoides (MF) or Sezary Syndrome (SS)

EXCLUSIONS:

- Hypersensitivity to mogamulizumab or any of the excipients
- Large cell transformation
- Clinical evidence of central nervous system (CNS) metastases
- Active autoimmune disease or infection
- Pregnancy
- Breastfeeding

CAUTION IN USE:

- Patients with cardiac disorders
- History of allogeneic transplant

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Haematologist working in the area of haematological malignancies.

TESTS:

Baseline tests:

- FBC, U&E's, renal and liver profile
- ECG, BNP for all patients and ECHO if previous cardiac history
- Virology screen - Hepatitis B* (HBsAg, HBcoreAb), Hepatitis C, HIV

*Hepatitis B reactivation: See Regimen Specific Complications

Regular tests:

- FBC, renal and liver profile prior to each cycle
- U&E's

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Dose reductions of mogamulizumab are not permitted, however dosing maybe interrupted for the management of adverse events induced by mogamulizumab. Please refer to Tables 1 and 2 below for the management of adverse events.

Renal and Hepatic Impairment:

Table 1: Dose modification of mogamulizumab in renal and hepatic impairment

Renal Impairment	Hepatic Impairment
Renal impairment: No dose adjustment is needed **Haemodialysis:** no dose adjustment is needed	**Mild and moderate:** no dose adjustment is needed **Severe:** no need for dose adjustment is expected

Management of adverse events:

Table 2: Management of skin reactions

Grade	Toxicity	Management
1	Rash covering <10% BSA with or without symptoms (e.g. pruritus, burning, tightness)	• Continue mogamulizumab • Treat with high potency Class 1 topical steroids and an antihistamine/other agent for pruritus (refer to local policy) • If rash does not improve, or worsens, refer for skin biopsy
2	• Rash covering 10-30% BSA with or without symptoms • Rash is limiting daily activities • Rash covering >30% BSA with or without mild symptoms	• Biopsy and referral to dermatology recommended • Hold mogamulizumab • Treat with high potency Class 1 topical steroids (refer to local policy) • Consider oral steroids (0.5 – 1 mg/kg/day)
3	• Rash covering >30% BSA with moderate or severe symptoms	
4	Life-threatening consequences; rash covering any % BSA, which may or may not be associated with symptoms of pruritus or tenderness and are associated with extensive superinfection with IV antibiotics indicated	• Discontinue mogamulizumab
Suspected Stevens Johnson Syndrome (SJS) or Toxic epidermal necrolysis (TEN)		• Mogamulizumab should be interrupted and treatment should not restart unless SJS or TEN is ruled out and cutaneous reaction has resolved to Grade 1 or less. • If SJS/TEN occur, appropriate medical therapy should be administered.

Table 3: Management of Infusion Related Reactions

Grade	Dose modification
1-3	Infusion should be temporarily disrupted and symptoms treated. The infusion rate should be reduced by at least 50% when re-starting the infusion after symptoms resolve. If reaction recurs, discontinuing the infusion should be considered.
4	Discontinue treatment

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

- As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting - Available on the NCCP website

Mogamulizumab: Low (**Refer to local policy).**

For information:
Within NCIS regimens, antiemetics have been standardised by Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

- Premedication with anti-pyretic and anti-histamine is recommended for the first mogamulizumab infusion.
- If an infusion related reaction occurs, administer premedication for subsequent mogamulizumab infusions.

Table 4: Suggested premedications prior to mogamulizumab infusion:

Drug	Dose	Route
Paracetamol	1000mg	PO 30 minutes prior to first mogamulizumab infusion. Only continue if infusion related reaction.
Chlorphenamine	10mg	IV bolus 30 minutes prior to first mogamulizumab infusion. Only continue if infusion related reaction.

OTHER SUPPORTIVE CARE:

- Tumour lysis syndrome prophylaxis **(Refer to local policy)**
- **Contraception:** Women of childbearing potential should use effective contraception during treatment with mogamulizumab and for at least 6 months after treatment.

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

REGIMEN SPECIFIC COMPLICATIONS:

- **Hepatitis B Reactivation:** Patients should be tested for both HBsAg and HBcoreAb as per local policy. If either test is positive, such patients should be treated with anti-viral therapy. **(Refer to local infectious disease policy).** These patients should be considered for assessment by hepatology.
- **Dermatological reactions:** Patients with MF or SS are susceptible to skin rashes and should be monitored throughout the course of treatment. Mogamulizumab can cause drug rash (drug eruption), sometimes of a severe nature, which may be mistakenly misinterpreted as progression of disease. The timing of any rash should be considered, with the median time to onset in the licensing MAVORIC trial being 15 weeks, and with 25 % of cases occurring after 31 weeks. Patients should be reviewed by both their dermatologist and haemato-oncologist and assessed/treated as per the recommendations in table 2.

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Kim YH, et al. Mogamulizumab versus vorinostat in previously treated cutaneous T-cell lymphoma (MAVORIC): an international, open-label, randomised, controlled phase 3 trial. Lancet oncol 2018; 19: 1192-204.
2. Musiek ACM, et al. Dermatologic Events Associated with the AntiCCR4 Antibody Mogamulizumab: Characterization and Management. Dermatol Ther (Heidelb). 2022 Jan;12(1):29-40.
3. Giraud E L, Lijster B D, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment: an update. Available at: https://pubmed.ncbi.nlm.nih.gov/37269847/
4. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V5 2023. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
5. Mogamulizumab Summary of Product Characteristics. Last updated: 06/09/2023. Accessed 11/03/2024. Available at https://www.ema.europa.eu/en/documents/product-information/poteligeo-epar-product-information_en.pdf

Version	Date	Amendment	Approved By
1	01/05/2023		Prof Elisabeth Vandenberghe and Lymphoid CAG
2	06/12/2024	Regimen reviewed. Updated dose modifications in renal and hepatic impairment as per Giraud et al (2023). History of allogeneic transplant moved from exclusions to cautions. Added table 2 for management of skin reactions. Added Table 3 suggested premedications. Updated regimen in line with NCCP standardisation.	Prof Elisabeth Vandenberghe and Lymphoid CAG

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.