Recommended by both NCCN[5] and NICE[6] guidelines*

MYLOTARG™
(gemtuzumab ozogamicin) INJECTION FOR IV INFUSION

POWER UP FOR LONGER REMISSION[1]

Adding MYLOTARG to chemotherapy delivered durable remission, as measured by EFS and RFS, in patients with newly diagnosed AML[1].

Median EFS of **17.3 months** vs 9.5 months (HR 0.56; P=0.0002) and **median RFS** of **28.0 months** vs 11.4 months (HR 0.53; P=0.0006) with **MYLOTARG plus chemotherapy** vs chemotherapy alone[1]

DOSING AND ADMINISTRATION GUIDE

INDICATION

MYLOTARG is indicated for combination therapy with daunorubicin (DNR) and cytarabine (AraC) for the treatment of patients aged 15 years and above with previously untreated, *de novo* CD33-positive acute myeloid leukaemia (AML), except acute promyelocytic leukaemia (APL)[2]

This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.

*NCCN: recommended for newly diagnosed patients with AML, in combination with daunorubicin and cytarabine[5]. NICE: recommended with daunorubicin and cytarabine, as an option in untreated *de novo* CD33-positive AML, except acute promyelocytic leukaemia, in people aged 15 years and over[6].

EFS, event-free survival; RFS, relapse-free survival.

Please see Important Safety Information on page 8, Section 4.8 of the Mylotarg Prescribing Information

Pfizer

BEFORE STARTING MYLOTARG

Premedication

- Premedication with a corticosteroid, antihistamine, and acetaminophen (or paracetamol) is recommended 1 hour prior to dosing[2].
- Appropriate measures to help prevent the development of tumour lysis-related hyperuricaemia, such as hydration, administration of antihyperuricemics (e.g., allopurinol) or other agents for treatment of hyperuricaemia (e.g., rasburicase) should be taken[2].

Cytoreduction

- In patients with hyperleukocytic (leukocyte count ≥30,000/mm^3) AML, cytoreduction is recommended 48 hours prior to administration of MYLOTARG[2].

HOW MYLOTARG IS SUPPLIED

MYLOTARG is supplied as a white to off-white cake or powder in a single-dose vial for concentrate for solution for infusion[2].

- Each vial delivers 5 mg gemtuzumab ozogamicin[2].
- Each carton contains one vial[2].

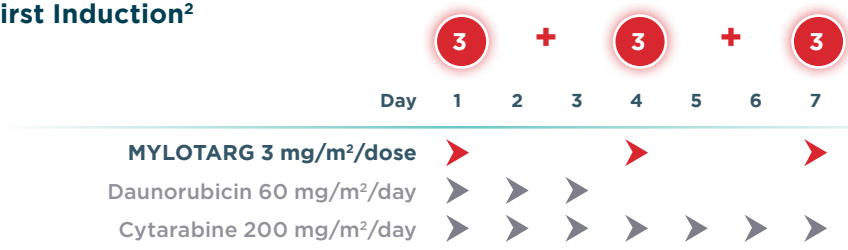
Please see Important Safety Information on page 8, Section 4.8 of the Mylotarg Prescribing Information

TREATMENT SCHEDULE

MYLOTARG Fractionated Dosing (3-3-3 Schedule)[2]

MYLOTARG should be used in combination with chemotherapy that consists of **one induction cycle and two consolidation cycles[2].**

First Induction[2]

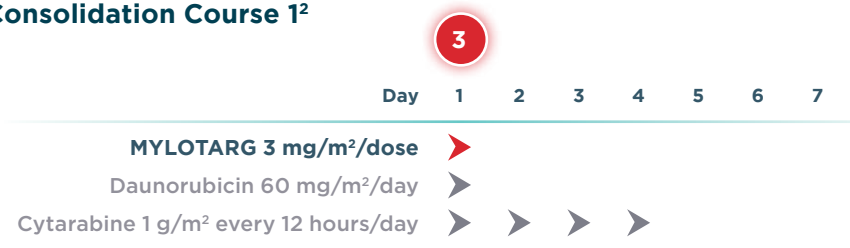


Adapted from MYLOTARG (gemtuzumab ozogamicin) Singapore Prescribing Information[2]

The recommended dose of MYLOTARG is 3 mg/m²/dose (**up to a maximum dose of one 5 mg vial**) infused over a 2-hour period on Days 1, 4 and 7 in combination with DNR 60 mg/m²/day infused over 30 minutes on Days 1 to 3, and AraC 200 mg/m²/day by continuous infusion on Days 1 to 7[2].

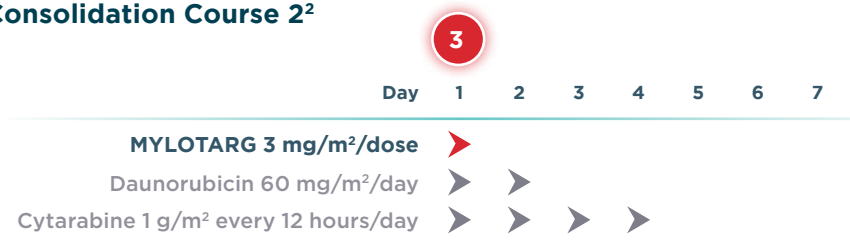
If a second induction course is required, **MYLOTARG should not be administered during this second induction** therapy[2].

Consolidation Course 1[2]



Adapted from MYLOTARG (gemtuzumab ozogamicin) Singapore Prescribing Information[2]

Consolidation Course 2[2]



Adapted from MYLOTARG (gemtuzumab ozogamicin) Singapore Prescribing Information[2]

The recommended dose of MYLOTARG is 3 mg/m²/dose (**up to a maximum dose of one 5 mg vial**) infused over a 2-hour period on Day 1 in combination with IV DNR (60 mg/m² for 1 day [first course] or 2 days [second course]) and IV AraC (1 g/m² every 12 hours, infused over 2 hours on Days 1 to 4)[2].

AraC, cytarabine; DNR, daunorubicin; IV, intravenous.

PREPARATION

Recommended dose of MYLOTARG is 3 mg/m²/dose (up to a maximum of one 5 mg vial)[2].

MYLOTARG is light sensitive and should be protected from light during reconstitution, dilution, and administration[2].

- If the product cannot be used immediately, the diluted solution may be stored up to 18 hours in a refrigerator (2°C–8°C) from the time of initial vial puncture with not more than 6 hours at room temperature (below 25°C)[2].
  - This includes the time required for reconstitution, dilution, and administration[2].

RECONSTITUTION

MYLOTARG is a cytotoxic drug. Follow applicable special handling and disposal procedures.

1. Calculate the dose (mg) of MYLOTARG required[2].
2. Prior to reconstitution, allow the vial to reach room temperature (below 25°C) for approximately 5 minutes. Reconstitute each 5 mg vial with 5 mL of water for injections to obtain a single-use solution of 1 mg/mL of gemtuzumab ozogamicin[2].
3. Gently swirl the vial to aid dissolution. **DO NOT SHAKE[2].**
4. Inspect the reconstituted solution for particulates and discoloration. The reconstituted solution may contain small white to off-white, opaque to translucent, and amorphous to fibre-like particles[2].

MYLOTARG contains no bacteriostatic preservatives. If the reconstituted solution cannot be used immediately, it may be stored in the original vial for up to 6 hours in a refrigerator (2°C–8°C) with not more than 3 hours at room temperature (below 25°C). Do not freeze[2].

Please see Important Safety Information on page 8, Section 4.8 of the Mylotarg Prescribing Information

DILUTION

1. Calculate the required volume of the reconstituted solution needed to obtain the appropriate dose according to patient body surface area (BSA). Withdraw this amount from the vial(s) using a syringe. **PROTECT FROM LIGHT[2].**
   - MYLOTARG vials contain 5 mg of drug product with no overfill. When reconstituted to a 1 mg/mL concentration as directed, the extractable content of the vial is 4.5 mg (4.5 mL)[2].
   - Discard any unused reconstituted solution left in the vial[2].
2. Doses must be mixed to a concentration between 0.075 mg/mL and 0.234 mg/mL according to the following instructions[2]:
   - Doses less than 3.9 mg must be prepared for administration by syringe. Add the reconstituted MYLOTARG solution to a syringe with sodium chloride 9 mg/mL (0.9%) solution for injection to a final concentration between 0.075 mg/mL and 0.234 mg/mL.
   - Doses greater than or equal to 3.9 mg are to be diluted in a syringe or an IV bag in an appropriate volume of sodium chloride 9 mg/mL (0.9%) solution for injection to ensure a final concentration between 0.075 mg/mL and 0.234 mg/mL. Protect from light.
3. Gently invert the infusion container to mix the diluted solution. **DO NOT SHAKE[2].**

The diluted solution should be used immediately or stored up to 6 hours at room temperature (below 25°C), including the 2-hour infusion time and 1 hour, if needed, to allow the refrigerated diluted solution to equilibrate to room temperature. The diluted solution can be refrigerated at 2°C–8°C for up to 12 hours. Do not freeze[2].

It is recommended that the infusion container be made of polyvinyl chloride (PVC) with DEHP, or polyolefin (polypropylene and/or polyethylene)[2].

ADMINISTRATION

MYLOTARG is administered by IV infusion over 2 hours. Pulse, blood pressure and temperature should be closely monitored during MYLOTARG infusion[2].

Administration Requirements	
Mode of Administration	IV infusion[2]
Infusion Time	2 hours[2]
Special Instructions	➤ During the infusion, the intravenous bag or syringes needs to be protected from light using a light (including ultraviolet light) blocking cover[2]. ➤ The infusion line does not need to be protected from light[2]. ➤ MYLOTARG should not be administered as an intravenous push or bolus[2].

Adapted from MYLOTARG (gemtuzumab ozogamicin) Singapore Prescribing Information[2]

Materials for Administration

- Filtration of the diluted solution is required. An in-line, low protein-binding 0.2 micron polyethersulphone (PES) filter must be used for infusion of MYLOTARG[2].
- Doses administered by syringe must utilize small bore infusion lines (microbore) with an in-line, low protein-binding 0.2 micron PES filter[2].
- Infusion lines made of PVC (DEHP- or non DEHP-containing), or polyethylene are recommended[2].

Do not mix MYLOTARG with, or administer as an infusion with, other medicinal products[2].

- Life-threatening or fatal infusion-related reactions can occur during or within 24 hours following infusion of MYLOTARG. Signs and symptoms of infusion-related reactions may include fever, chills, hypotension, tachycardia, and respiratory symptoms[2].
- Premedicate prior to MYLOTARG infusion. Monitor vital signs frequently during infusion. Interrupt infusion immediately for patients who develop evidence of infusion reaction, especially dyspnoea, bronchospasm, or hypotension. Monitor patients until signs and symptoms completely resolve[2].
- Discontinue use of MYLOTARG in patients who develop signs or symptoms of anaphylaxis, including severe respiratory symptoms or clinically significant hypotension[2].

Please see Important Safety Information on page 8, Section 4.8 of the Mylotarg Prescribing Information

STORING UNUSED MYLOTARG

- Refrigerate (2°C–8°C) MYLOTARG vials and store in the original carton to protect from light[2].
- DO NOT FREEZE[2].

HANDLING RECONSTITUTED AND DILUTED MYLOTARG SOLUTION

The following time intervals for reconstitution, dilution, and administration should be followed for storage of the reconstituted solution[2].

Handling MYLOTARG

Reconstituted Solution	Diluted Solution	
	After Dilution	Administration
➤ If the reconstituted solution cannot be used immediately, it may be stored in the original vial for up to 6 hours in a refrigerator (2°C–8°C) with not more than 3 hours at room temperature (below 25°C)[2]. ➤ **PROTECT FROM LIGHT[2].** ➤ **DO NOT FREEZE[2].**	➤ If not used immediately, store at room temperature (below 25°C) for up to 6 hours, which includes the 2-hour infusion time and 1 hour, if needed, to allow the refrigerated diluted solution to equilibrate to room temperature[2]. ➤ The diluted solution can be refrigerated at 2°C–8°C for up to 12 hours[2]. ➤ **PROTECT FROM LIGHT[2].** ➤ **DO NOT FREEZE[2].**	2-hour infusion[2]

Adapted from MYLOTARG (gemtuzumab ozogamicin) Singapore Prescribing Information[2]

- Total maximum hours from reconstitution to end of administration: 18 hours[2].
- Maximum time at room temperature following dilution: 6 hours[2].

DOSE MODIFICATIONS FOR HAEMATOLOGICAL TOXICITIES

Dose modification of MYLOTARG is recommended based on individual safety and tolerability[2].

Haematological Toxicities	
Criteria	**Recommended Actions**
Persistent Thrombocytopenia (Defined as Platelets <100,000/mm^3 at the **Planned Start Date of the Consolidation Course**)	➤ If platelet count does not to greater than or equal to 100,000 mm3 within 14 days following the planned start date of the consolidation cycle (14 days after hematologic recovery following previous cycle), discontinue MYLOTARG (do not administer MYLOTARG in the consolidation cycles)
Persistent Neutropenia	➤ If neutrophil count does not recover to greater than 500/mm^3 within 14 days following the planned start date of the consolidation cycle (14 days after haematologic recovery following previous cycle), discontinue MYLOTARG (do not administer MYLOTARG in the consolidation cycles)[2].

Adapted from MYLOTARG (gemtuzumab ozogamicin) Singapore Prescribing Information[2]

AraC, cytarabine; BMA, bone marrow aspirate; DNR, daunorubicin.

Please see Important Safety Information on page 8, Section 4.8 of the Mylotarg Prescribing Information

DOSE MODIFICATIONS FOR NON-HAEMATOLOGICAL TOXICITIES

Non-Haematological Toxicities

Criteria	Recommended Actions
VOD/SOS	➤ Discontinue MYLOTARG and treat patient according to standard medical practice[2].
Total Bilirubin >2 × ULN, and AST and/or ALT >2.5 × ULN	➤ Postpone MYLOTARG until recovery of total bilirubin to ≤2 × ULN and AST and ALT to ≤2.5 × ULN prior to each dose[2]. ➤ Consider omitting scheduled dose if delayed more than 2 days between sequential infusions[2].
Infusion-Related Reactions	➤ Interrupt the infusion and institute appropriate medical management based on the severity of symptoms[2]. ➤ Patients should be monitored until signs and symptoms completely resolve and infusion may resume[2]. ➤ Consider permanent discontinuation of treatment for severe or life-threatening infusion reactions[2].
Other Severe or Life-Threatening Non-Haematologic Toxicities	➤ Delay treatment with MYLOTARG until recovery to a severity of no more than 'mild'[2]. ➤ Consider omitting scheduled dose if delayed more than 2 days between sequential infusions[2].

Adapted from MYLOTARG (gemtuzumab ozogamicin) Singapore Prescribing Information[2]

ALT, alanine transaminase; AST, aspartate aminotransferase; SOS, sinusoidal obstruction syndrome; ULN, upper limit of normal; VOD, veno-occlusive disease.

1

Fractionated dosing of MYLOTARG delivers **efficacy without excessive toxicity** and demonstrates a **favourable benefit/risk profile**[1,3]

- MYLOTARG treatment before alloHCT is **not associated with increased risk of post-transplant VOD or death**[7]

2

With MYLOTARG, patients achieved **superior event-free and relapse-free survival**[2]

- **mEFS** and **mRFS** were **17.3 months** and **28.0 months**, respectively, in the MYLOTARG plus chemotherapy arm compared to 9.5 months and 11.4 months, respectively, in the chemotherapy alone arm[1]

3

Targets CD33, expressed in **up to 90% of AML** cases[4]

4

No additional hospital stays required with MYLOTARG because it is administered as a 2-hour infusion[2]

5

MYLOTARG plus chemotherapy is recommended by the **NCCN** and **NICE guidelines** for AML

- Recommended for newly diagnosed *de novo* AML in NCCN Guidelines[5]
- Recommended as an option for untreated *de novo* CD33+ AML in NICE Guideline[6]

alloHCT, allogeneic hematopoietic cell transplantation; AML, acute myeloid leukaemia; mEFS, median event-free survival; mRFS, median relapse-free survival; NCCN, National Comprehensive Cancer Network; NICE, National Institute for Health and Care Excellence.

Please see Important Safety Information on page 8, Section 4.8 of the Mylotarg Prescribing Information

WARNING: Hepatotoxicity, including severe or fatal hepatic veno-occlusive disease (VOD), also known as sinusoidal obstruction syndrome (SOS), has been reported in association with the use of MYLOTARG as part of a combination chemotherapy regimen. Monitor frequently for signs and symptoms of VOD/SOS after treatment with MYLOTARG.

Contraindications: Hypersensitivity to MYLOTARG or any of its components. Reactions have included anaphylaxis.

Hepatotoxicity, Including Hepatic VOD/SOS: Hepatotoxicity, including life-threatening, and sometimes fatal hepatic failure and VOD/SOS have been reported in patients treated with MYLOTARG. Based on an analysis of potential risk factors, adult patients who received MYLOTARG as monotherapy, either before or after an haematopoietic stem cell transplant (HSCT), and patients with moderate or severe hepatic impairment are at increased risk for developing VOD. Due to the risk of VOD/SOS, signs and symptoms of VOD/SOS should be closely monitored; these may include elevations in ALT, AST, total bilirubin, and alkaline phosphatase, which should be monitored prior to each dose of MYLOTARG, hepatomegaly (which may be painful), rapid weight gain, and ascites. Monitoring only total bilirubin may not identify all patients at risk of VOD/SOS. For patients who develop abnormal liver tests, more frequent monitoring of liver tests and clinical signs and symptoms of hepatotoxicity is recommended. For patients who proceed to HSCT, close monitoring of liver tests is recommended during the post-HSCT period, as appropriate. No definitive relationship was found between VOD and time of HSCT relative to higher MYLOTARG monotherapy doses, however, the ALFA-0701 study recommended an interval of 2 months between the last dose of MYLOTARG and HSCT. Management of signs or symptoms of hepatic toxicity may require a dose interruption, or discontinuation of MYLOTARG. In patients who experience VOD/SOS, MYLOTARG should be discontinued and patients treated according to standard medical practice.

Infusion-Related Reactions (Including Anaphylaxis): In clinical studies infusion related reactions, including anaphylaxis were reported. There have been reports of fatal infusion reactions in the post-marketing setting. Signs and symptoms of infusion related reactions may include fever and chills, and less frequently hypotension, tachycardia, and respiratory symptoms that may occur during the first 24 hours after administration. Infusion of MYLOTARG should be performed under close clinical monitoring, including pulse, blood pressure, and temperature. Premedication with a corticosteroid, antihistamine and acetaminophen (or paracetamol) is recommended 1 hour prior to MYLOTARG dosing. Infusion should be interrupted immediately for patients who develop evidence of severe reactions, especially dyspnoea, bronchospasm, or clinically significant hypotension. Patients should be monitored until signs and symptoms completely resolve. Discontinuation of treatment should be strongly considered for patients who develop signs or symptoms of anaphylaxis, including severe respiratory symptoms or clinically significant hypotension.

Myelosuppression: In clinical studies, neutropenia, thrombocytopenia, anaemia, leukopenia, febrile neutropenia, lymphopenia, and pancytopenia, some of which were life-threatening or fatal, were reported. Complications associated with neutropenia and thrombocytopenia may include infections and bleeding/haemorrhagic reactions respectively. Infections and bleeding/haemorrhagic reactions were reported, some of which were life-threatening or fatal. Complete blood counts should be monitored prior to each dose of MYLOTARG. During treatment, patients should be monitored for signs and symptoms of infection, bleeding/haemorrhage, or other effects of myelosuppression. Routine clinical and laboratory surveillance testing during and after treatment is indicated. Management of patients with severe infection, bleeding/haemorrhage, or other effects of myelosuppression, including severe neutropenia or persistent thrombocytopenia, may require a dose delay or permanent discontinuation of MYLOTARG.

Adverse Cytogenetics: The efficacy of MYLOTARG has been shown in AML patients with favourable- and intermediate-risk cytogenetics, with uncertainty regarding the size of the effect in patients with adverse cytogenetics. For patients being treated with MYLOTARG in combination with daunorubicin and cytarabine for newly diagnosed *de novo* AML, when cytogenetics testing results become available it should be considered whether the potential benefit of continuing treatment with MYLOTARG outweighs the risks for the individual patient.

Embryo-Foetal Toxicity: There are no or limited amount of data from the use of MYLOTARG in pregnant women. Studies in animals have shown reproductive toxicity. MYLOTARG must not be used during pregnancy unless the potential benefit to the mother outweighs the potential risks to the foetus. Pregnant women, or patients becoming pregnant whilst receiving MYLOTARG, or treated male patients as partners of pregnant women, must be apprised of the potential hazard to the foetus. Women of childbearing potential, or partners of females of childbearing potential should be advised to use 2 methods of effective contraception during treatment with MYLOTARG for at least 7 months (females) or 4 months (males) after the last dose.

Adverse Reactions: In the combination therapy study ALFA-0701, clinically relevant serious adverse reactions were hepatotoxicity, including VOD/SOS (3.8%), haemorrhage (9.9%), severe infection (41.2%), and tumour lysis syndrome (1.5%). In monotherapy studies, clinically relevant serious adverse reactions also included infusion related reactions (2.5%), thrombocytopenia (21.7%), and neutropenia (34.3%).

References: 1. Lambert J, Pautas C, Terré C, et al. Gemtuzumab ozogamicin for de novo acute myeloid leukemia: final efficacy and safety updates from the open-label, phase III ALFA-0701 trial. Haematologica. 2019;104(1):113–119; with supplementary data available at: http://www.haematologica.org/content/haematol/suppl/2019/01/07/haematol.2018.188888.DC2/2018.188888.LAMBERT_SUPPL.pdf. Accessed Oct 2021. **2.** MYLOTARG Prescribing Information. Pfizer Singapore. Version Jun 2021. **3.** Castaigne S, Pautas C, Terré C, et al. Effect of gemtuzumab ozogamicin on survival of adult patients with de-novo acute myeloid leukaemia (ALFA-0701): a randomised, open-label, phase 3 study. Lancet. 2012;379(9825):1508– 1516. **4.** Ehninger A, Kramer M, Röllig C, et al. Distribution and levels of cell surface expression of CD33 and CD123 in acute myeloid leukemia. Blood Cancer J. 2014;4:e218. **5.** Acute Myeloid Leukemia, Version 3.2020, NCCN Clinical Practice Guidelines in Oncology. Available at: https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed Oct 2021. **6.** Gemtuzumab ozogamicin for untreated acute myeloid leukaemia, November 2018 NICE Technology appraisal guidance [TA545]. Available at: https://www.nice.org.uk/guidance/ta545/chapter/1-Recommendations. Accessed Oct 2021. **7.** Ho VT, Martin AS, P.rez WS, et al. Prior Gemtuzumab Ozogamicin Exposure in Adults with Acute Myeloid Leukemia Does Not Increase Hepatic Veno-Occlusive Disease Risk after Allogeneic Hematopoietic Cell Transplantation: A Center for International Blood and Marrow Transplant Research Analysis. Biology of Blood and Marrow Transplantation. 2020;26(5):884–892.

To access the MYLOTARG (gemtuzumab ozogamicin)Prescribing Information, please scan the QR code or visit: http://labeling.pfizer.com/ShowLabeling. aspx?id=15470

For Healthcare Professionals Only

Pfizer Private Limited
180 Pasir Panjang Road, #16-81/82, Mapletree Business City, Singapore 117372
Tel: +65-6403 8888 Fax: +65-6403 8868 Website: www.pfizer.com.sg

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MYLOTARG™
(gemtuzumab ozogamicin) INJECTION FOR IV INFUSION