A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Astellas Ireland Co. Ltd
Killorglin
Co. Kerry
Ireland

B. CONDITIONS OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product subject to restricted medical prescription (See Annex I: Summary of Product Characteristics, section 4.2).

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

The MAH shall ensure that prior to launch of the product prescribers will receive the prescriber checklist in order to ensure that:

- Mycamine is contra-indicated if the patient has a history of hypersensitivity to micafungin or excipients.
- Mycamine should not be used during pregnancy unless clearly necessary.
- Caution must be demonstrated if the patient:
  - has severe liver function impairment
  - has chronic liver diseases known to represent preneoplastic conditions (e.g. advanced liver fibrosis, cirrhosis, viral hepatitis, neonatal liver disease or congenital enzyme defects)
  - is receiving a concomitant therapy including hepatotoxic and/or genotoxic properties
  - has history of haemolysis, haemolytic anaemia or renal impairment.
- Patients receiving sirolimus, nifedipine or itraconazole in combination with Mycamine should be monitored for sirolimus, nifedipine or itraconazole toxicity and the sirolimus, nifedipine or itraconazole dosage should be reduced if necessary.
- Patients should be carefully monitored for liver damage and for worsening of renal function.
- To minimise the risk of adaptive regeneration and potentially subsequent liver tumour formation, early discontinuation in the presence of significant and persistent elevation of ALT/AST is recommended.

- **OTHER CONDITIONS**

Pharmacovigilance system
The MAH must ensure that the system of pharmacovigilance, as described in version 4 presented in Module 1.8.1. of the Marketing Authorisation Application, is in place and functioning before and whilst the product is on the market.

Risk Management Plan
The MAH commits to performing the studies and additional pharmacovigilance activities detailed in the Pharmacovigilance Plan, as agreed in version 5.0 of the Risk Management Plan (RMP) presented in Module 1.8.2. of the Marketing Authorisation Application and any subsequent updates of the RMP agreed by the CHMP.

As per the CHMP Guideline on Risk Management Systems for medicinal products for human use, the updated RMP should be submitted at the same time as the next Periodic Safety Update Report (PSUR).

In addition, an updated RMP should be submitted

- When new information is received that may impact on the current Safety Specification, Pharmacovigilance Plan or risk minimisation activities
- Within 60 days of an important (pharmacovigilance or risk minimisation) milestone being reached
- At the request of the EMA

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Mycamine 50 mg powder for solution for infusion

Micafungin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains: 50 mg micafungin (as sodium).
After reconstitution each ml contains 10 mg of micafungin (as sodium).

3. LIST OF EXCIPIENTS

Lactose monohydrate, citric acid anhydrous and sodium hydroxide.
See the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous infusion after reconstitution and dilution.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Astellas Pharma Europe B.V.
Elisabethhof 19
2353 EW Leiderdorp
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/08/448/001

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Mycamine 50 mg powder for solution for infusion
Micafungin
Intravenous use.

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

50 mg

6. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

CARTON

1. NAME OF THE MEDICINAL PRODUCT

Mycamine 100 mg powder for solution for infusion

Micafungin

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each vial contains: 100 mg micafungin (as sodium).
After reconstitution each ml contains 20 mg of micafungin (as sodium).

3. LIST OF EXCIPIENTS

Lactose monohydrate, citric acid anhydrous and sodium hydroxide.
See the package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

1 vial

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For intravenous infusion after reconstitution and dilution.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP:

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Astellas Pharma Europe B.V.
Elisabethhof 19
2353 EW Leiderdorp
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/08/448/002

13. BATCH NUMBER

Lot:

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

VIAL

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

Mycamine 100 mg powder for solution for infusion
Micafungin
Intravenous use.

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP:

4. BATCH NUMBER

Lot:

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

100 mg

6. OTHER

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

Mycamine 50 mg powder for solution for infusion
Mycamine 100 mg powder for solution for infusion
Micafungin

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT MYCAMINE IS AND WHAT IT IS USED FOR

Mycamine is called an antifungal medicine because it is used to treat infections caused by fungal cells. Mycamine is used to treat fungal infections caused by fungal or yeast cells called Candida. Mycamine is effective in treating systemic infections (those that have penetrated within the body). It interferes with the production of a part of the fungal cell wall. An intact cell wall is necessary for the fungus to continue living and growing. Mycamine causes defects in the fungal cell wall, making the fungus unable to live and grow.

Your doctor has prescribed Mycamine for you in the following circumstances when there are no other suitable antifungal treatments available (see section 2):

- To treat adults, adolescents and children who have a serious fungal infection called invasive candidiasis (infection that has penetrated the body).
- To treat adults and adolescents ≥ 16 years of age who have a fungal infection in the gullet (oesophagus) where treatment into a vein (intravenous) is appropriate.
- To treat adults, adolescents and children who are at risk of developing a Candida fungal infection that may penetrate the body.

2. BEFORE YOU USE MYCAMINE

Do not use Mycamine
- if you are allergic (hypersensitive) to micafungin or any of the other ingredients of Mycamine.

Take special care with Mycamine

In rats, long-term treatment with micafungin led to liver damage and subsequent liver tumours. The potential risk of developing liver tumours in humans is not known, and your doctor will assess the benefits and risks of Mycamine treatment before starting your medicine. Please tell your doctor if you have severe liver problems (e.g. liver failure or hepatitis) or have had abnormal liver function tests. During treatment your liver functions will be monitored more closely.

- if you have haemolytic anaemia (anaemia due to breakdown of red blood cells) or haemolysis (breakdown of red blood cells).
- if you have kidney problems (e.g. kidney failure and abnormal kidney function test). If this happens, your doctor may decide to monitor your kidney function more closely.

Using other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

It is especially important to inform your doctor if you are using amphotericin B desoxycholate or itraconazole (antifungal antibiotics), sirolimus (an immunosuppressant) or nifedipine (a calcium antagonist). Your doctor may decide to adjust the dose of these medicines.

Using Mycamine with food and drink
As Mycamine is given intravenously (into a vein), no restrictions on food or drink are required.

Pregnancy and breast-feeding
Ask your doctor or pharmacist for advice before taking any medicine.
Mycamine should not be used during pregnancy unless clearly necessary. If you use Mycamine you should not breast-feed.

Driving and using machines
There is no information on the effect of Mycamine on the ability to drive or use machines. Please inform your doctor if you experience any effects that may cause you to have problems with driving or using other machinery.

Important information about some of the ingredients of Mycamine
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW TO USE MYCAMINE

Mycamine must be prepared and given to you by a doctor or another health care professional.
Mycamine should be administered once daily by slow intravenous (into a vein) infusion. Your doctor will determine how much Mycamine you will receive each day.

Use in adults, adolescents ≥ 16 years of age and elderly
- The usual dose to treat an invasive Candida infection is 100 mg per day for patients weighing 40 kg or more and 2 mg/kg per day for patients weighing 40 kg or less.
- The dose to treat a Candida infection of the oesophagus is 150 mg for patients weighing more than 40 kg and 3 mg/kg per day for patients weighing 40 kg or less.
- The usual dose to prevent invasive Candida infections is 50 mg per day for patients weighing more than 40 kg and 1 mg/kg per day for patients weighing 40 kg or less.

Use in children (including newborns) and adolescents < 16 years of age
- The usual dose to treat an invasive Candida infection is 100 mg per day for patients weighing 40 kg or more and 2 mg/kg per day for patients weighing 40 kg or less.
- The usual dose to prevent invasive Candida infections is 50 mg per day for patients weighing more than 40 kg and 1 mg/kg per day for patients weighing 40 kg or less.

If you receive more Mycamine than you should
Your doctor monitors your response and condition to determine what dose of Mycamine is needed. However, if you are concerned that you may have been given too much Mycamine, speak to your doctor or another health care professional immediately.

If you miss a dose of Mycamine

Your doctor monitors your response and condition to determine what Mycamine treatment is needed. However, if you are concerned that you may have missed a dose, speak to your doctor or another health care professional immediately.

Effects when treatment with Mycamine is stopped
There are no known withdrawal symptoms.

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Mycamine can cause side effects, although not everybody gets them.

The safety of Mycamine has been assessed in clinical trials. Patients in these trials were critically ill, had a wide variety of other medical conditions, and required many other medicines.

Mycamine may cause the following side effects:

Common (affects 1 to 10 users in 100)
- abnormal blood tests (decreased white blood cells [leucopenia; neutropenia]); decreased red blood cells (anaemia)
- decreased potassium in the blood (hypokalaemia); decreased magnesium in the blood (hypomagnesaemia); decreased calcium in the blood (hypocalcaemia)
- headache
- inflammation of the vein wall (at injection-site)
- nausea (feeling sick); vomiting (being sick); diarrhoea; abdominal pain
- abnormal liver function tests (increased alkaline phosphatase; increased aspartate aminotransferase, increased alanine aminotransferase)
- increased bile pigment in the blood (hyperbilirubinaemia)
- rash
- fever
- rigors (shivering)

Uncommon (affects 1 to 10 users in 1,000)
- abnormal blood tests (decreased blood cells [pancytopenia]); decreased blood platelets (thrombocytopenia); increases in a certain type of white blood cells called eosinophils; decreased albumin in the blood (hypoalbuminaemia)
- allergic attack (anaphylactic reaction / anaphylactoid shock); hypersensitivity
- increased sweating
- decreased sodium in the blood (hyponatraemia); increased potassium in the blood (hyperkalaemia); decreased phosphates in the blood (hypophosphataemia); anorexia (eating disorder)
- insomnia (difficulty in sleeping); anxiety; confusion
- feeling lethargic (somnolence); trembling; dizziness; disturbed taste
- increased heart rate; stronger heartbeat; irregular heartbeat
- high or low blood pressure; skin flushing
- shortness of breath
- indigestion; constipation
- liver failure; increased liver enzymes (gamma-glutamyltransferase); jaundice (yellowing of the skin or whites of the eyes caused by liver or blood problems); reduced bile reaching the intestine (cholestasis); enlarged liver; liver inflammation
- itchy rash (urticaria); itching; skin flushing (erythema)
- abnormal kidney function tests (increased blood creatinine; increased urea in the blood); aggravated kidney failure
- increase in an enzyme called lactate dehydrogenase

- clotting in vein at injection-site; inflammation at injection-site; pain at injection-site; collection of fluid in your body

Rare (affects 1 to 10 users in 10,000)
- anaemia due to breakdown of red blood cells (haemolytic anaemia), breakdown of red blood cells (haemolysis)

Not known (frequency cannot be estimated from the available data)
- shock
- damage to liver cells including death
- severe skin reaction
- kidney problems; acute kidney failure

The following reactions have been reported more often in paediatric patients than in adult patients:
Common (affects 1 to 10 users in 100)
- decreased blood platelets (thrombocytopenia)
- increased heart rate (tachycardia)
- high or low blood pressure
- increased bile pigment in the blood (hyperbilirubinaemia); enlarged liver
- acute kidney failure; increased urea in the blood

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE MYCAMINE

Keep out of the reach and sight of children.

Do not use Mycamine after the expiry date which is stated on the vial and on the carton. The expiry date refers to the last day of that month.

The unopened vial does not require any special storage conditions.
The reconstituted concentrate and the diluted infusion solution should be used immediately.

Do not use the diluted infusion solution if it is cloudy or precipitated.

In order to protect the infusion bottle / bag containing the diluted infusion solution from light it should be inserted into a closable opaque bag.

The vial is for single use only. Therefore, please discard unused reconstituted concentrate immediately.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

Reconstituted Mycamine should be used immediately because it does not contain any preservatives to prevent bacterial contamination. Only a trained health care professional who has read the complete directions properly can prepare this medicine for use.

6. FURTHER INFORMATION

What Mycamine contains

- The active substance is micafungin sodium.
  1 vial contains 50 mg or 100 mg micafungin (as sodium).

- The other ingredients are lactose monohydrate, citric acid anhydrous and sodium hydroxide.

What Mycamine looks like and contents of the pack

Mycamine 50 mg or 100 mg powder for solution for infusion is a white compact freeze-dried powder. Mycamine is supplied in a box containing 1 vial.

Marketing Authorisation Holder
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Netherlands

Manufacturer
Astellas Ireland Co., Ltd.
Killorglin, County Kerry
Ireland

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last approved in {MM/YYYY}.

Detailed information on this medicine is available on the European Medicines Agency (EMA) web site: http://www.ema.europa.eu/.

The following information is intended for medical or healthcare professionals only:

Mycamine must not be mixed or co-infused with other medicinal products except those mentioned below. Using aseptic techniques at room temperature, Mycamine is reconstituted and diluted as follows:

1. The plastic cap must be removed from the vial and the stopper disinfected with alcohol.
2. Five ml of sodium chloride 9 mg/ml (0.9%) solution for infusion or glucose 50 mg/ml (5%) solution for infusion (taken from a 100 ml bottle/bag) should be aseptically and slowly injected into each vial along the side of the inner wall. Although the concentrate will foam, every effort should be made to minimise the amount of foam generated. A sufficient number of vials of Mycamine must be reconstituted to obtain the required dose in mg (see table below).
3. The vial should be rotated gently. DO NOT SHAKE. The powder will dissolve completely. The concentrate should be used immediately. The vial is for single use only. Therefore, please discard unused reconstituted concentrate immediately.
4. All of the reconstituted concentrate should be withdrawn from each vial and returned into the infusion bottle/bag from which it was originally taken. The diluted infusion solution should be used immediately. Chemical and physical in-use stability have been demonstrated for 96 hours at 25°C when protected from light and diluted as described above.
5. The infusion bottle/bag should be gently inverted to disperse the diluted solution but NOT agitated in order to avoid foaming. Do not use if the solution is cloudy or has precipitated.
6. The infusion bottle/bag containing the diluted infusion solution should be inserted into a closable opaque bag for protection from light.

Preparation of the solution for infusion

Dose (mg)	**Mycamine vial to be used (mg/vial)**	**Volume of sodium chloride (0.9%) or glucose (5%) to be added per vial**	**Volume (concentration) of reconstituted powder**	**Standard infusion (added up to 100 ml) Final concentration**
50	1 x 50	5 ml	approx. 5 ml (10 mg/ml)	0.5 mg/ml
100	1 x 100	5 ml	approx. 5 ml (20 mg/ml)	1.0 mg/ml
150	1 x 100 + 1 x 50	5 ml	approx. 10 ml	1.5 mg/ml
200	2 x 100	5 ml	approx. 10 ml	2.0 mg/ml

ANNEX IV

CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT TO BE IMPLEMENTED BY THE MEMBER STATES