This item forms part of the Risk Management Materials for Maacy® (macitentan)

Maacy®

Macitentan 10mg
film coated tablet

Frequently asked questions brochure for healthcare professionals

This Document is approved by Executive Directorate of Pharmacovigilance at Saudi Food & Drug Authority (SFDA)

SPC سدير للأدوية

Version: 0.1
Date: July.2022

Contents

		Page
1	What is the purpose of this brochure?	3
2	What is **Maacy**®?	3
3	What is **Maacy**® indicated for?	3
4	What dose of **Maacy**® should be used?	3
5	Should the dose of Maacy® be adjusted for patients with hepatic or renal impairment or the elderly?	4
6	When is **Maacy**® contraindicated?	4
7	What are the main risks associated with the use of **Maacy**®?	4
8	How can the risk of anaemia be prevented and managed?	4
9	What should I know about the risk of teratogenicity associated with **Maacy**®, and how can it be prevented?	5
10	What is meant by women of childbearing potential?	5
11	What should I consider before prescribing **Maacy**® to a woman of childbearing potential?	5
12	What is considered a reliable method of contraception?	6
13	What should I do if a patient taking **Maacy**® becomes pregnant?	6
14	What should I know about the risk of hepatotoxicity associated with **Maacy**®?	6
15	What other important safety information should I be aware of in order to minimise the risks associated with **Maacy**®?	7
16	What should I discuss with my patients, and what assessments need to be performed before initiating treatment with Maacy®?	7
17	How is **Maacy**® supplied?	7
18	How should **Maacy**® be stored?	8
19	What is the role of the prescribing checklist?	8
20	What is the patient card?	8
21	Where can I obtain further information?	8
22	How can I obtain additional copies of the tools?	8
23	Reporting of adverse drug reactions and pregnancies	8
24	Notes	9

1. What is the purpose of this brochure?

These frequently asked questions (FAQs) are provided by Sudair Pharma for prescribers and other healthcare professionals (HCPs) who are involved in the treatment of patients on **Maacy**® for whom you have determined are capable of complying with the requirements for the safe use of **Maacy**®.

Treatment with **Maacy**® should only be initiated and monitored by a physician experienced in the treatment of pulmonary arterial hypertension (PAH).

This document will enable you to:

- Understand what **Maacy**® is used for and how it should be used
- Learn about identified risks associated with **Maacy**®, and how they should be prevented and managed
- Understand potential side effects of **Maacy**® and how they should be prevented
- Provide important safety information to patients

This document summarises the most important information about **Maacy**®. Please also familiarise yourself with the complete Summary of Product Characteristics (SmPC) before prescribing or dispensing **Maacy**®.

2. What is Maacy®?

Endothelin (ET-1) and its receptors (ETA and ETB) mediate a variety of effects such as vasoconstriction, fibrosis, proliferation, hypertrophy and inflammation. In disease conditions such as PAH, the local ET system is upregulated and is involved in vascular hypertrophy and in organ damage.

Maacy® is an orally active potent endothelin receptor antagonist, active on both ETA and ETB receptors and approximately 100-fold more selective for ETA as compared to ETB in vitro. **Maacy**® displays high affinity and sustained occupancy of the ET receptors in human pulmonary arterial smooth muscle cells. This prevents endothelin-mediated activation of second messenger systems that result in vasoconstriction and smooth muscle cell proliferation.

3. What is Maacy® indicated for?

Maacy®, as monotherapy or in combination, is indicated for the long-term treatment of pulmonary arterial hypertension (PAH) in adult patients of WHO Functional Class II to III.

Efficacy has been shown in a PAH population including idiopathic and heritable PAH, PAH associated with connective tissue disorders and PAH associated with corrected simple congenital heart disease.

4. What dose of Maacy® should be used?

Maacy® should be taken orally at a dose of 10 mg once daily with or without food. Tablets are not breakable and should be taken whole, with water.v

Maacy® should be taken every day at about the same time. If the patient misses a dose of **Maacy**®, the patient should be told to take it as soon as possible and then take the next dose at the regularly scheduled time. The patient should be told not to take two doses at the same time if a dose has been missed.

5. Should the dose of Maacy® be adjusted for patients with hepatic or renal impairment or the elderly?

Based on pharmacokinetic (PK) data, no dose adjustment is required in patients with mild, moderate or severe hepatic impairment. There is no clinical experience with the use of **Maacy**® in PAH patients with moderate or severe hepatic impairment. **Maacy**® must not be initiated in patients with severe hepatic impairment or clinically significant elevated hepatic aminotransferases (greater than 3 times the Upper Limit of Normal (>3 x ULN); see sections 4.3 and 4.4 of the SmPC).

Based on PK data, no dose adjustment is required in patients with renal impairment. There is no clinical experience with the use of **Maacy**® in PAH patients with severe renal impairment.

Caution is recommended in this population. The use of **Maacy**® is not recommended in patients undergoing dialysis.

No dose adjustment is required in patients aged over 65 years. There is limited clinical experience in patients aged over 75 years. Therefore **Maacy**® should be used with caution in this population.

6. When is Maacy® contraindicated?

Maacy® is contraindicated in:

- Patients with hypersensitivity to the active substance, soya or to any of the excipients listed in section 6.1 of the SmPC. Please note that the tablets contain lactose
- Pregnant women
- Women of child-bearing potential who are not using reliable contraception
- Breastfeeding women
- Patients with severe hepatic impairment
- Patients with baseline values of hepatic aminotransferases (aspartate aminotransferases [AST] and/or alanine aminotransferases [ALT] >3× ULN)

7. What are the main risks associated with the use of Maacy®?

As with other ERAs, treatment with **Maacy**® is associated with a risk of anaemia, teratogenicity and hepatotoxicity.

8. How can the risk of anaemia be prevented and managed?

Decrease in haemoglobin concentrations has been associated with endothelin receptor antagonists (ERAs) including **Maacy**® (see section 4.8). In placebo-controlled studies, **Maacy**® related decreases in haemoglobin concentration were not progressive, stabilised after the first 4–12 weeks of treatment and remained stable during chronic treatment. Cases of anaemia requiring blood cell transfusion have been reported with **Maacy**® and other ERAs.

Initiation of **Maacy**® is not recommended in patients with severe anaemia.

It is recommended that haemoglobin concentrations be measured prior to initiation of treatment and tests repeated during treatment as clinically indicated.

If tests show a clinically significant decrease in haemoglobin or haematocrit, other causes should be excluded.

Please report clinically significant decreases in haemoglobin or haematocrit and adverse events to Sudair Pharma Company. Reporting can be done via telephone: +966-920001432 ext.107 or by email: pharmacovigilance@sudairpharma.com

9. What should I know about the risk of teratogenicity associated with Maacy®, and how can it be prevented?

There is no specific data or relevant clinical experience with respect to the teratogenic potential of **Maacy**® in the human foetus. However, developmental and reproductive toxicity studies in rabbits and rats showed that **Maacy**®® is teratogenic at all doses tested in these animal species. In both species there were cardiovascular and mandibular arch fusion abnormalities.

The risk for humans remains unknown but appropriate precautions must be taken for women of childbearing potential. **Maacy**® is contraindicated during pregnancy and in women of childbearing potential who are not using reliable contraception. **Maacy**® treatment should only be initiated in women of childbearing potential when the absence of pregnancy has been verified.

Monthly pregnancy tests in women of childbearing potential being treated with **Maacy**® are recommended to allow early detection of pregnancy.

Women should not become pregnant for 1 month after discontinuation of **Maacy**®.

10. What is meant by women of childbearing potential?

"Woman of childbearing potential" means any woman who does not meet at least one of the following criteria:

- Aged at least 50 years and naturally amenorrhoeic for at least 1 year (amenorrhoea following cancer therapy does not rule out child-bearing potential)
- Premature ovarian failure, confirmed by a specialist gynaecologist
- Other documented impairment of oviductal or uterine function that would cause sterility
- Previous bilateral salpingo-oophorectomy, or hysterectomy
- XY genotype, Turner syndrome, or uterine agenesis

Women with oligomenorrhea, women who are peri-menopausal and young females who have begun to menstruate are considered to be of childbearing potential.

11. What should I consider before prescribing Maacy® to a woman of childbearing potential?

Women of childbearing potential should not start treatment with **Maacy**® unless:

- The absence of pregnancy has been verified
- Advice on contraception has been provided
- They are using a reliable method of contraception
- They continue to use reliable contraception while taking **Maacy**® and for one month after treatment discontinuation

Monthly pregnancy tests are recommended.

12 What is considered a reliable method of contraception?

The following are considered reliable methods of contraception:

- Oral contraceptive, either combined or progestogen alone
- Injectable progestogen
- Implants of levonorgestrel
- Oestrogenic vaginal ring
- Percutaneous contraceptive patches
- Intrauterine device (IUD) or intrauterine system (IUS)
- Male partner sterilisation (vasectomy with documentation of azoospermia)
- Tubal ligation
- Double barrier method: condom and occlusive cap (diaphragm or cervical/vault caps) plus vaginal spermicidal agent (foam, gel, film, cream or suppository)
- No male partner

13. What should I do if a patient taking Maacy® becomes pregnant?

If a pregnancy occurs during **Maacy**® therapy, the risks to the foetus should be discussed with the patient and a decision taken whether to discontinue treatment, taking into account also the risk to the mother due to PAH. Consideration should be given as to whether it is appropriate to refer the patient to a Consultant specialised in teratology and its diagnosis for further education and advice.

Patients should be told to report immediately any possible pregnancy that occurs during **Maacy**® use.

If a pregnancy occurs during **Maacy**® therapy, please inform Sudair Pharma Company via telephone: +966-920001432 ext.107 or email pharmacovigilance@sudairpharma.com. All cases of pregnancy should be reported to Sudair Pharma.

14. What should I know about the risk of hepatotoxicity associated with Maacy®?

Elevations of liver aminotransferases (ALT, AST) have been associated with PAH and with endothelin receptor antagonists (ERAs).

Maacy® is not to be initiated in patients with severe hepatic impairment or elevated aminotransferases (>3 x ULN) and is not recommended in patients with moderate hepatic impairment.

Liver enzyme tests should be obtained prior to initiation of **Maacy**®.

Patients should be monitored for signs of hepatic injury and monthly monitoring of ALT and AST is recommended. If sustained, unexplained, clinically relevant aminotransferase elevations occur, or if elevations are accompanied by an increase in bilirubin >2 x ULN, or by clinical symptoms of liver injury (e.g., jaundice), **Maacy**® treatment should be discontinued.

Re-initiation of **Maacy**® may be considered following the return of hepatic enzyme levels to within the normal range in patients who have not experienced clinical symptoms of liver injury. The advice of a hepatologist is recommended.

Please report clinically significant elevations of ALT and/or AST, or any other liver related adverse events to Sudair Pharma Company Reporting can be done via

Telephone: +966-920001432 ext.107 or by pharmacovigilance@sudairpharma.com.

15. What other important safety information should I be aware of in order to minimise the risks associated with Maacy®?

Patients with renal impairment may run a higher risk of experiencing hypotension and anaemia during treatment with **Maacy®**®. Therefore, monitoring of blood pressure and haemoglobin should be considered.

Cases of pulmonary oedema have been reported with vasodilators (mainly prostacyclins) when used in patients with pulmonary veno-occlusive disease. Consequently, if signs of pulmonary oedema occur when **Maacy®** is administered in patients with PAH, the possibility of pulmonary veno-occlusive disease should be considered.

In the presence of strong CYP3A4 inducers reduced efficacy of **Maacy®** could occur. The combination of **Maacy®** with strong CYP3A4 inducers (e.g., rifampicin, St. John's wort, carbamazepine, and phenytoin) should be avoided.

Caution should be exercised when **Maacy®** is administered concomitantly with strong CYP3A4 inhibitors (e.g., itraconazole, ketoconazole, voriconazole, clarithromycin, telithromycin, nefazodone, ritonavir, and saquinavir).

There is limited clinical experience in patients over the age of 75 years, and therefore **Maacy®** should be used with caution in this population.

Maacy® tablets contain lactose monohydrate. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Maacy® tablets contain lecithin derived from soya. If a patient is hypersensitive to soya, **Maacy®** must not be used.

16. What should I discuss with my patients, and what assessments need to be performed before initiating treatment with Maacy®?

A pregnancy test, liver function tests and measure of haemoglobin concentrations should be performed before initiation of treatment with **Maacy®**. Your role in educating patients about their new therapy and its possible effects and side effects is very important. You will need to inform patients about the important side effects associated with **Maacy®**, teach patients how to recognise relevant symptoms and signs of side effects, and inform patients of the need to report any side effect that may occur to the prescribing physician immediately.

You also need to inform female patients of childbearing potential of the risks to the foetus in case of pregnancy both from PAH and from **Maacy®**, and of the need to:

- Use a reliable method of contraception
- Have monthly pregnancy tests
- Report pregnancy immediately if it occurs

It is very important that you remind the patient about this important safety information regularly during their treatment with **Maacy®**.

17. How is Maacy® supplied?

Maacy® is available in the form of white, biconvex, round film-coated tablets with “10" on both sides. **Maacy®** is supplied in blister packs of 30 film-coated tablets.

18. How should Maacy® be stored?

Maacy® must be stored at a temperature not exceeding 30˚C. Unexposed tablets have a shelf life of 5 years.

19. What is the role of the prescribing checklist?

The prescribing checklist is a tool designed to help you identify key risk information that should be evaluated and discussed with the patient before prescribing **Maacy**®.

The completed checklist can be stored with the patient chart as helpful evidence that the patient has been informed of the risks associated with treatment with **Maacy**®.

20. What is the patient card?

The patient card is a small, folding, credit-card sized card, which should be carried by the patients at all times and will contain key information about their treatment:

- A reminder of the need to report immediately any pregnancy or side effect that may occur during treatment
- Information regarding precautions to be taken to minimise the risk of teratogenicity,
- i.e. the need to:
  - use a reliable method of contraception
  - have monthly pregnancy tests
  - report pregnancy immediately if it occurs
- Information regarding the risks of anaemia and hepatotoxicity, and in particular the importance to contact the prescribing physician in case the patient experiences symptoms of liver injury
- Key information about how to take **Maacy**®
- Name and contact details of the prescribing physician

21. Where can I obtain further information?

For further information, please refer to the SmPC.

22. How can I obtain additional copies of the tools?

Patient card, prescribing checklist and frequently asked questions brochure for healthcare professionals are available electronically on https://www.sfda.gov.sa/en/RMM?keys=%20Maacy®&tags=All&field_risk_minimization_type=All

Further hard copies of all educational materials can be requested by emailing pharmacovigilance@sudairpharma.com

23. Reporting of adverse drug reactions and pregnancies

Please report suspected adverse drug reactions (ADRs) to Saudi Food and Drug Authority (SFDA) via:

- website: https://ade.sfda.gov.sa
- email: npc.drug@sfda.gov.sa
- Call center: 19999

Also, you can report to Sudair Pharma Company vis:

Phone:920001432,ext.107
Fax:00966114668195
Email: Pharmacovigilance@SudairPharma.com

When reporting please provide as much information as possible. By reporting side effects, you can help provide more information on the safety of this medicine.

In addition, all AE's and cases of pregnancy should be reported to Sudair Pharma.

Reporting can be done via telephone: +966-920001432 ext.107 or by email: pharmacovigilance@sudairpharma.com.

For further information, please refer to the SPC.

24. Notes

Maacy®

Macitentan 10mg
film coated tablet

SPC
سدير للأدوية

Mail to: Riyadh Gallery Mall, Building A2,
Office 305-A, Riyadh, Saudi Arabia
Phone: 920001432, ext. 107
Fax: 00966 11 4668195
Email: Pharmacovigilance@SudairPharma.com
www.SudairPharma.com

Version: 0.1
Date: July.2022