Please also read carefully the Summary of Product Characteristics before prescribing Daxas®.

Daxas ▼® (roflumilast) in your practice
Information for prescribers

▼ This medicine is subject to additional monitoring. The purpose of this monitoring is to allow quick identification of new safety information. Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form, which is available online at http://www.medicinesauthority.gov.mt/adrportal, and sent by post or email to;

P: Pharmacovigilance Section at Post-Licensing Directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000

E: postlicensing.medicinesauthority@gov.mt

Adverse events should also be reported to AstraZeneca on **00356 2277 8115**. This includes any side effects not listed in this document. Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. By reporting side effects, you can help provide more information on the safety of this medicine.

What is Daxas®?

Daxas® contains the active substance roflumilast, which is a phosphodiesterase 4 (PDE4) inhibitor, a non-steroid, anti-inflammatory active substance designed to target both the systemic and the pulmonary inflammation associated with chronic obstructive pulmonary disease (COPD).

For which patients should I prescribe Daxas®?

Daxas® is indicated for maintenance treatment of severe COPD (FEV1 post-bronchodilator less than 50% predicted) associated with chronic bronchitis in adult patients with a history of frequent exacerbations as add on to bronchodilator treatment.

How is Daxas® administered?

· The recommended starting dose is one tablet of Daxas® 250 micrograms once daily for 28 days,

· After 28 days patients must be up-titrated to one tablet of Daxas® 500 micrograms once daily,

· Doses to be taken at the same time every day with water, with or without food.

(*The 250 micrograms starting dose is intended to reduce adverse events and patient discontinuation when initiating therapy, but it is a sub-therapeutic dose*)

Daxas® is a regular treatment and targets the underlying chronic inflammation. Therefore, it may need to be taken for several weeks to achieve its effects. You may want to inform your patient about this fact.

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For which patients should I NOT prescribe Daxas®?

Daxas® is not indicated for:

· patients under 18 years of age,
· COPD patients other than indicated,
· relief of acute bronchospasms,
· the treatment of asthma,
· the treatment of genetic alpha-1-antitrypsin deficiency.

Contraindications

· Hypersensitivity to roflumilast or to any of the excipients.
· Moderate or severe liver impairment (Child-Pugh B or C).

Precautions

Patients should be informed about precautions for safe use and the risks of Daxas®. Please also hand out the patient card, which can be downloaded from the Medicines Authority website (www.medicinesauthority.gov.mt)

Due to lack of experience, Daxas® should not be initiated or should be stopped in patients who have or develop:

· severe immunological diseases (e.g. HIV infection, multiple sclerosis, lupus erythematosus, progressive multifocal leukoencephalopathy)
· severe acute infectious diseases
· cancers (except basal cell carcinoma)
· current immunosuppressive therapy other than short-term systemic corticosteroids

Experience in patients with latent infections such as tuberculosis, viral hepatitis, herpes viral infection and herpes zoster is limited.

Patients with congestive heart failure (NYHA grades 3 and 4) have not been studied and therefore treatment of these patients is not recommended.

The clinical data with Daxas® in patients with mild hepatic impairment classified as Child-Pugh A are insufficient to recommend a dose adjustment and therefore Daxas® should be used with caution in these patients.

Weight Decrease

In 1-year studies, a decrease of body weight occurred more frequently in patients treated with Daxas® compared to placebo-treated patients. After discontinuation of Daxas®, the majority of patients had regained body weight after 3 months.

In patients who are underweight, body weight should be measured at each visit. Patients should be advised to check their body weight every two weeks and record the results on the patient information card. In the event of an unexplained and clinically concerning weight decrease, intake of Daxas® should be discontinued and body weight should be further followed up.

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Psychiatric disorders

Daxas® is associated with an increased risk of psychiatric disorders such as insomnia, anxiety, nervousness and depression. Rare instances of suicidal ideation and behaviour, including suicide, have been observed in patients with or without a history of depression, usually within the first weeks of treatment. The risks and benefits of starting or continuing treatment with Daxas® should be carefully assessed if patients report previous or existing psychiatric symptoms or if concomitant treatment with other medicinal products likely to cause psychiatric events is intended. Daxas® is not recommended in patients with a history of depression associated with suicidal ideation or behavior. If patients suffered from new or worsening psychiatric symptoms, or suicidal ideation or suicidal attempt is identified, it is recommended to discontinue treatment with Daxas®.

Patients and caregivers should be advised to report any changes in the patient's mood or behaviour as well as any occurrence of suicidal ideation.

Persistent intolerability and increased exposure in certain populations

While adverse reactions like diarrhoea, nausea, abdominal pain and headache mainly occur within the first weeks of therapy and mostly resolve on continued treatment, Daxas® treatment should be reassessed in case of persistent intolerability. This might be the case in special populations that may have higher exposure, such as in black, non-smoking females or in patients concomitantly treated with CYP1A2/2C19/3A4 inhibitors (such as fluvoxamine and cimetidine) or CYP1A2/3A4 inhibitors (such as enoxacin).

Theophylline

There are no clinical data to support the concomitant treatment with theophylline for maintenance therapy. Therefore, the concomitant treatment with theophylline is not recommended.

Adverse Events

Please refer to section 4.8 of the Summary of Product Characteristics (SmPC) for Daxas® for information on the incidence of undesirable effects.

Reference: SmPC for Daxas film-coated tablets, available on the Medicines Authority website (www.medicinesauthority.gov.mt).

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Daxas® roflumilast

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