Before prescribing Daxas®, please read the Summary of Product Characteristics carefully.

Daxas® 500 mcg Film-coated Tablets (roflumilast)▼ in your practice

▼ This medicinal product is subject to additional monitoring. 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. Healthcare professionals are asked to report any suspected adverse reactions to HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; Email: medsafety@hpra.ie.

Information for prescribers

What is Daxas®?
Daxas® contains the active substance roflumilast which is a selective phosphodiesterase 4 (PDE4) inhibitor that targets both the systemic and the pulmonary inflammation associated with COPD.

Which patients are suitable for Daxas®?
Daxas® is indicated for maintenance treatment of severe chronic obstructive pulmonary disease (COPD) (FEV1 post-bronchodilator less than 50% predicted) associated with chronic bronchitis in adult patients with a history of frequent exacerbations, as an add on to bronchodilator treatment.¹

There are no data to support the use of Daxas® in children and adolescents under 18 years of age.

How is Daxas® administered?
The recommended dose is:
· one Daxas® 500 microgram tablet per day taken with water, with or without food.
Daxas® is a regular treatment and targets the underlying chronic inflammation. It may therefore need to be taken for several weeks before the desired effects are achieved. You may want to inform your patient about this.

Which patients should NOT be prescribed Daxas®?
· patients under 18 years of age,
· COPD patients other than those indicated above,
· the relief of acute bronchospasms,
· the treatment of asthma,
· the treatment of genetic alpha-1-antitrypsin deficiency.

Treatment with Daxas® should not be initiated or existing treatment with Daxas® should be stopped in patients with:
· severe immunological diseases (e.g. HIV infection, multiple sclerosis, lupus erythematosus, progressive multifocal leukoencephalopathy)
· severe acute infectious diseases (e.g. acute hepatitis)
· cancer (except basal cell carcinoma)
· current immunosuppressive therapy other than short-term systemic corticosteroids

Contraindications
· in patients with hypersensitivity to roflumilast or to any of the excipients,
· in patients with moderate or severe liver impairment (Child-Pugh B or C).
Precautions
Before starting treatment with Daxas®, patients should be informed about precautions for safe use and the risks associated with Daxas®.

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 (M2-124, M2-125), a decrease of body weight occurred more frequently in patients with Daxas® compared to placebo-treated patients. After discontinuation of Daxas®, the majority of patients had regained body weight after 3 months.

Body weight of underweight patients should be checked at each visit. Patients should be advised to check their body weight on a regular basis and record the results on the Patient 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.

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 completed suicide, have been observed in patients with or without a history of depression, usually in 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 behaviour. Patients and caregivers should be instructed to notify their prescriber of any changes in behaviour or mood and of any suicidal ideation.

If patients suffer from new or worsening psychiatric symptoms, or suicidal thoughts or a 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 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 concomitant treatment with theophylline for maintenance therapy. Therefore, concomitant treatment with theophylline is not recommended.

References:
1. Takeda GmbH. Daxas® Summary of Product Characteristics

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DAXAS® ▼ (roflumilast)
ABBREVIATED SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

Refer to full SmPC before prescribing

**Presentation:** Film-coated Tablets: 500 micrograms of roflumilast.

**Indication:** Maintenance treatment of severe chronic obstructive pulmonary disease (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. **Dosage & Administration:** One tablet daily, swallowed with water, taken at the same time every day. Daxas needs to be taken for several weeks to achieve its effect. **Hepatic impairment:** Mild hepatic impairment - use with caution; moderate or severe hepatic impairment - do not take Daxas. **Renal impairment and Elderly:** No dose adjustment necessary. **Children:** There is no relevant use of Daxas in the paediatric population. **Contraindications:** Hypersensitivity. Moderate or severe hepatic impairment (Child-Pugh B or C). **Warnings & Precautions:** Patients should be informed about the risks and precautions and should be given a patient card before starting Daxas. Rescue medicine: Daxas is not for the relief of acute bronchospasm. Weight decrease: Weight loss can occur. Body weight of underweight patients should be checked at each visit and patients advised to check their weight regularly. Daxas should be stopped and the patient followed up if weight loss is unexplained and clinically concerning. Special clinical conditions: Due to lack of relevant experience, do not use Daxas in patients with severe immunological diseases (e.g. HIV infection, multiple sclerosis, lupus erythematosus, progressive multifocal leukoencephalopathy), severe acute infectious diseases, cancers (except basal cell carcinoma), congestive heart failure (NYHA grades 3 and 4) or patients treated with immunosuppressives (i.e. methotrexate, azathioprine, infliximab, etanercept, or oral long-term corticosteroids). Experience in patients with latent infections such as tuberculosis, viral hepatitis, herpes viral infection and herpes zoster is limited. **Psychiatric disorders:** Daxas is associated with increased risk of psychiatric disorders such as insomnia, anxiety, nervousness and depression. Rare instances of suicidal ideation and behaviour, including completed suicide, may be observed. The risks and benefits of Daxas should be carefully assessed if patients report previous or existing psychiatric symptoms or if patients are concomitantly treated with other medicinal products likely to cause psychiatric events. Patients and caregivers should be instructed to notify the prescriber of any changes in behaviour or mood and of any suicidal ideation. Daxas is not recommended in patients with a history of depression associated with suicidal ideation or behaviour. Daxas should be discontinued if patients suffer from new or worsening psychiatric symptoms, or if suicidal ideation or suicide attempt is identified. Persistent intolerability: 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 (especially in populations that may have higher exposure e.g. black, non-smoking females, or patients concomitantly treated with fluvoxamine, enoxacin or cimetidine). **Theophylline:** Concomitant treatment with theophylline is not recommended due to lack of data. Lactose: Daxas tablets contain lactose. Patients with galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take Daxas. **Interactions:** Daxas is metabolised by CYP3A4 and CYP1A2. Interaction studies with CYP3A4 inhibitors erythromycin and ketoconazole, CYP1A2 inhibitors fluvoxamine and dual CYP 3A4/1A2 inhibitors enoxacin and cimetidine resulted in increases in total PDE4 inhibitory activity. Therefore concomitant use of Daxas with these may lead to an increase in exposure and persistent intolerability in which case Daxas treatment should be reassessed. Cytochrome P450 enzyme inducer rifampicin caused a reduction in total PDE4 inhibitory activity, therefore concomitant use of strong cytochrome P450 inducers e.g. phenobarbital, carbamazepine, phenytoin may reduce the therapeutic efficacy of roflumilast. Co-administration with theophylline or an oral contraceptive containing gestodene and ethinyl oestradiol caused an increase in total PDE4 inhibitory activity. No interactions were observed with inhaled salbutamol, formoterol, budesonide and oral montelukast, digoxin, warfarin, sildenafil, midazolam and an antacid (combination of aluminium hydroxide and magnesium hydroxide). **Fertility, Pregnancy & Lactation:** Daxas is not recommended during pregnancy or in women of childbearing potential not using contraception and should not be used during breastfeeding. In a human spermatogenes is study 500mg roflumilast had no effect on semen parameters or reproductive hormones. **Undesirable Effects:** Common (≥1/100 to <1/10): weight decreased, decreased appetite, insomnia, headache, diarrhoea, nausea and abdominal pain. Other serious undesirable effects: Uncommon (≥1/1,000 to <11/100): hypersensitivity; Rare (≥1/10,000 to <1/1,000): suicidal ideation and behaviour, depression, blood creatine phosphokinase (CPK) increased, angioedema. Refer to the full SmPC for details on full side effect profile and interactions.

**Marketing Authorisation Number:** EU/1/10/636/002: 30 tablet pack; EU/1/10/636/003: 90 tablet pack. The full SmPC is available from Takeda UK Ltd, Building 3, Glory Park, Glory Park Avenue, Wooburn Green, Buckinghamshire, HP10 0DF. Tel +44 (0)1628 537900. Fax +44 (0)1628 526617

Adverse Events should be reported to the Pharmacovigilance Unit at the Healthcare Products Regulatory Agency (HPRA) (medsafety@hpra.ie). Information about Adverse Event reporting can be found on the HPRA website (www.hpra.ie). Adverse Events should also be reported to Takeda UK Ltd on 1800 937 970.