Adenuric (febuxostat) 80 mg and 120 mg film-coated tablets
Prescribing Information
Please consult the Summary of Product Characteristics (SmPC) for full prescribing information.
Presentation: Film-coated tablets containing 80 mg or 120 mg febuxostat. Also contains lactose monohydrate.
Use: Treatment of chronic hyperuricaemia in conditions where urate deposition has already occurred (including a history or presence of, tophus and/or gouty arthritis) in adults. Adenuric 120 mg is also indicated for the prevention and treatment of hyperuricaemia in adult patients undergoing chemotherapy for haematologic malignancies at intermediate to high risk of Tumor Lysis Syndrome (TLS).
Dosage and administration: Oral use with or without food. Recommended dose: *Gout:* 80 mg once daily. If serum uric acid is > 6 mg/dL (357 µmol/l) after 2-4 weeks, 120 mg once daily may be considered. *Prevention and treatment of hyperuricaemia in patients at risk of TLS* - 120 mg once daily. Start two days before beginning of cytotoxic therapy and continue for a minimum of 7 days; treatment may be prolonged up to 9 days according to chemotherapy duration as per clinical judgment. *Older people:* No dose adjustment required. *Renal impairment:* No dosage adjustment necessary in patients with mild or moderate renal impairment. Efficacy and safety not fully evaluated in patients with severe renal impairment. *Hepatic impairment:* Recommended dosage in patients with mild hepatic impairment is 80 mg. Limited information available in patients with moderate hepatic impairment. Efficacy and safety has not been studied in patients with severe hepatic impairment. *Children and adolescents:* Safety and efficacy in children under 18 has not been established. *Organ transplant recipients:* No experience therefore not recommended.
Contra-indications: Hypersensitivity to the active ingredient or to any of the excipients.
Warnings and precautions: *Cardio-vascular disorders: Treatment of chronic hyperuricaemia:*
Not recommended in patients with pre-existing major cardiovascular diseases (e.g. myocardial infarction, stroke or unstable angina), unless no other therapy options are appropriate. *Prevention and treatment of hyperuricaemia in patients at risk of TLS:* Cardiac monitoring of patients undergoing chemotherapy for haematologic malignancies at intermediate to high risk of Tumor Lysis. *Product allergy/hypersensitivity:* Advise patients of signs/symptoms of allergic/hypersensitivity reactions and monitor closely for symptoms. Stop treatment immediately if serious reactions occur, including Stevens-Johnson syndrome, toxic epidermal necrolysis and acute anaphylactic reaction/shock; do not re-start febuxostat at any time. Severe hypersensitivity reactions, including Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) associated with fever, haematological, renal or hepatic involvement in some cases. *Acute gouty attacks (gout flare):* Do not start treatment until an acute attack of gout has completely subsided. As with other urate lowering medicinal products, gout flares may occur during initiation of treatment. At treatment initiation flare prophylaxis for at least 6 months with an NSAID or colchicine is recommended. If a gout flare occurs during treatment do not discontinue. Manage the gout flare concurrently as appropriate. Continuous treatment decreases frequency and intensity of gout flares. *Xanthine deposition:* As with other urate lowering medicinal products, in patients in whom the rate of urate formation is greatly increased (e.g. malignant disease and its treatment, Lesch-Nyhan syndrome), the absolute concentration of xanthine in urine could, in rare cases, rise sufficiently to allow deposition in the urinary tract. Not observed in pivotal clinical study in TLS. As there has been no experience of its use in patients with Lesch-Nyhan Syndrome its use is not recommended. *Mercaptopurine/azathioprine:* Not recommended in patients concomitantly treated with mercaptopurine/azathioprine. Where combination cannot be avoided, monitor patients closely. Dose reduction for mercaptopurine/azathioprine is recommended. *Theophylline:* No pharmacokinetic interaction shown with febuxostat 80 mg, no data for 120 mg. *Liver disorders:* Liver function test is recommended prior to the initiation of therapy and periodically thereafter, based on clinical judgement. *Thyroid disorders:* Caution in patients with alteration of thyroid function. *Lactose:* Contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

Interactions: *Mercaptopurine/azathioprine:* On the basis of the mechanism of action of febuxostat on xanthine oxidase inhibition concomitant use is not recommended. Where the combination cannot be avoided see SmPC for dosing instructions. *Rosiglitazone/CYP2C8 inhibitors:* No dosage adjustment required. *Theophylline:* No special caution advised for 80 mg febuxostat, no data available for 120 mg. *Naproxen and other inhibitors of glucuronidation:* Can be co-administered with naproxen with no dose adjustments necessary. *Inducers of glucuronidation:* Monitoring of serum uric acid is recommended 1-2 weeks after start of treatment with a potent inducer of glucuronidation. Cessation of treatment of an inducer might lead to increased plasma levels of febuxostat.
Colchicine/indometacin/hydrochlorothiazide/warfarin: Can be co-administered with colchicine or indomethacin with no dose adjustments necessary. No dose adjustment necessary when administered with hydrochlorothiazide. No dose adjustment necessary for warfarin when administered with febuxostat. *Desipramine/CYP2D6 substrates:* Co-administration with other CYP2D6 substrates is not expected for those compounds. *Antacids:* May be taken without regard to antacid use.
Pregnancy and Lactation: Do not use during pregnancy or breast-feeding. Effect on fertility unknown.
Side-effects: *Clinical Studies and post-marketing experience in gout patients:* Common (1-10%): Gout flares, headache, diarrhoea*, nausea, liver function test abnormalities*, rash, oedema. Uncommon (0.1–1%): Blood thyroid stimulating hormone increased, diabetes mellitus, hyperlipidemia, decrease appetite, weight increase, decreased libido, insomnia, dizziness, paraesthesia, hemiparesis, somnolence, altered taste, hypoaesthesia, hyposmia, atrial fibrillation, palpitations, ECG abnormal, left bundle branch block (TLS study), sinus tachycardia (TLS study), hypertension, flushing, hot flush, haemorrhage (TLS study), dyspnoea, bronchitis, upper respiratory tract infection, cough, abdominal pain, abdominal distension, gastro-oesophageal reflux disease, vomiting, dry mouth, dyspepsia, constipation, frequent stools, flatulence, gastrointestinal discomfort, cholelithiasis, dermatitis, urticaria, pruritus, skin discolouration, skin lesion, petechiae, rash macular, rash maculopapular, rash papular, arthralgia, arthritis, myalgia, musculoskeletal pain, muscle weakness, muscle spasm, muscle tightness, bursitis, renal failure, nephrolithiasis, haematuria, pollakiuria, proteinuria, erectile dysfunction, fatigue, chest pain, chest discomfort, blood amylase increase, platelet count decrease, WBC decrease, lymphocyte count decrease, blood creatine increase, blood creatinine increase, haemoglobin decrease, blood urea increase, blood triglycerides increase, blood cholesterol increase, haematocritic decrease, blood lactate dehydrogenase increased, blood potassium increase. Rare (0.1-0.01%): Pancytopenia, thrombocytopenia, agranulocytosis**, anaphylactic reaction**, drug hypersensitivity**, blurred vision, weight decrease, increase appetite, anorexia, nervousness, tinnitus, sudden cardiac death**, pancreatitis, mouth ulceration, hepatitis, jaundice**, liver injury**, Toxic epidermal necrolysis**, Stevens-Johnson Syndrome**, DRESS**, angioedema**, generalized rash (serious)**, erythema, exfoliative rash, rash follicular, rash vesicular, rash pustular, rash pruritic**, rash erythematous, rash morbillifom, alopecia, hyperhidrosis, rhabdomyolysis**, joint stiffness, musculoskeletal stiffness, tubulointerstitial nephritis**, micturition urgency, thirst, blood glucose increase, activated partial thromboplastin time prolonged, red blood cell count decrease, blood alkaline phosphatase increase, blood creatine phosphokinase increase**. *Treatment-emergent non-infective diarrhoea and abnormal liver function tests in combined Phase III studies more frequent in patients concomitantly treated with colchicine. **Adverse reactions coming from post-marketing experience. Rare serious hypersensitivity reactions including Stevens-Johnson Syndrome and anaphylactic reaction/shock have occurred in post-marketing experience. Hypersensitivity reactions to febuxostat can be associated with the following symptoms: skin reactions characterised by infiltrated maculopapular eruption, generalised or exfoliative rashes, also skin lesions, facial oedema, fever, haematologic abnormalities such as thrombocytopenia and eosinophilia, and single or multiple organ involvement (liver and kidney including tubulointerstitial nephritis). Gout flares commonly observed soon after treatment start and in first months. Frequency decreases after time. Gout flare prophylaxis is recommended.
Please consult the SmPC for further information.
Package quantities and price: 80 mg tablets: 28 film-coated tablets: £24.36; 120 mg tablets: 28 film-coated tablets: £24.36.

Legal category: POM
Marketing authorization number: EU/1/08/447/014, 020.
Marketing authorization holder: Menarini International Operations Luxembourg S.A. 1 Avenue de la Gare, L-1611 Luxembourg.
Marketed by: A. Menarini Farmaceutica Internazionale SRL.
Further information is available on request to A. Menarini Farmaceutica Internazionale SRL, Menarini House, Mercury Park, Wycombe Lane, Wooburn Green, Buckinghamshire, HP10 0HH or may be found in the SmPC.
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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to A. Menarini Farmaceutica Internazionale SRL. Phone no. 0800 085 8678 or email: menarini@medinformation.co.uk