Prescribing Information

Docetaxel Accord 20/1, 80/4, 160mg/8ml concentrate for solution for infusion

Please refer to the Summary of Product Characteristics (SmPC) before prescribing.

Presentation: Each ml of concentrate contains 20mg docetaxel.

Indications: *Breast cancer:* in combination with doxorubicin and cyclophosphamide for the adjuvant treatment of patients with operable node-positive breast cancer or operable node-negative breast cancer. For patients with operable node-negative breast cancer, adjuvant treatment should be restricted to patients eligible to receive chemotherapy according to internationally established criteria for primary therapy of early breast cancer. *Additional indications:* in combination with doxorubicin for the treatment of patients with locally advanced or metastatic breast cancer who have not previously received cytotoxic therapy for this condition; as monotherapy for the treatment of patients with locally advanced or metastatic breast cancer after failure of cytotoxic therapy (previous chemotherapy should have included an anthracycline or an alkylating agent); in combination with trastuzumab for the treatment of patients with metastatic breast cancer whose tumours over express HER2 and who previously have not received chemotherapy for metastatic disease; in combination with capecitabine for the treatment of patients with locally advanced or metastatic breast cancer after failure of cytotoxic chemotherapy (previous therapy should have included an anthracycline). *Non-small cell lung cancer:* for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior chemotherapy; in combination with cisplatin for the treatment of patients with unresectable, locally advanced or metastatic non-small cell lung cancer, in patients who have not previously received chemotherapy for this condition. *Prostate cancer:* in combination with prednisone or prednisolone for the treatment of patients with metastatic castration-resistant prostate cancer; in combination with androgen-deprivation therapy (ADT), with or without prednisone or prednisolone, for the treatment of patients with metastatic hormone-sensitive prostate cancer. *Gastric adenocarcinoma:* in combination with cisplatin and 5-fluorouracil for the treatment of patients with metastatic gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for metastatic disease. *Head and neck cancer*: in combination with cisplatin and 5-fluorouracil for the induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck.

Dosage and Administration: The use of docetaxel should be confined to units specialised in the administration of cytotoxic chemotherapy and it should only be administered under the supervision of a physician qualified in the use of anticancer chemotherapy. *Posology:* For breast, non-small cell lung, gastric, and head and neck cancers, premedication consisting of an oral corticosteroid, such as dexamethasone 16 mg per day (e.g. 8 mg twice daily) for 3 days starting 1 day prior to docetaxel administration, unless contraindicated, can be used. For metastatic castration-resistant prostate cancer, given the concurrent use of prednisone or prednisolone, the recommended premedication regimen is oral dexamethasone 8 mg, 12 hours, 3 hours and 1 hour before the docetaxel infusion. For metastatic hormone-sensitive prostate cancer, irrespective of the concurrent use of prednisone or prednisolone, the recommended premedication regimen is oral dexamethasone 8 mg 12 hours, 3 hours, and 1 hour before docetaxel infusion. Prophylactic G-CSF may be used to mitigate the risk of haematological toxicities. Docetaxel is administered as a one-hour infusion every three weeks. *Breast cancer:* In the adjuvant treatment of operable node-positive and node-negative breast cancer, the recommended dose of docetaxel is 75 mg/m^2 administered 1-hour after doxorubicin 50 mg/m^2 and cyclophosphamide 500 mg/m^2 every 3 weeks for 6 cycles (TAC regimen). For the treatment of patients with locally advanced or metastatic breast cancer, 100 mg/m^2 in monotherapy. In first-line treatment, docetaxel 75 mg/m^2 is given in combination therapy with doxorubicin (50 mg/m^2). In combination with trastuzumab, docetaxel 100 mg/m^2 every three weeks, with trastuzumab administered weekly. In combination with capecitabine, docetaxel 75 mg/m^2 every three weeks, combined with capecitabine at 1250 mg/m^2 twice daily (within 30 minutes after a meal) for 2 weeks followed by a 1-week rest period. *Non-small cell lung cancer:* In chemotherapy naïve patients treated for non-small cell lung cancer, the recommended dose of docetaxel is 75 mg/m^2 immediately followed by cisplatin 75 mg/m^2 over 30-60 minutes. For treatment after failure of prior platinum-based chemotherapy, the

recommended dose of docetaxel is 75 mg/m^2 as a single agent. *Metastatic castration-resistant prostate cancer:* the recommended dose of docetaxel is 75 mg/m^2. Prednisone or prednisolone 5 mg orally twice daily is administered continuously. *Metastatic hormone-sensitive prostate cancer:* the recommended dose of docetaxel is 75 mg/m^2 every 3 weeks for 6 cycles. Prednisone or prednisolone 5 mg orally twice daily may be administered continuously. *Gastric adenocarcinoma:* the recommended dose of docetaxel is 75 mg/m^2 as a 1-hour infusion, followed by cisplatin 75 mg/m^2, as a 1- to 3-hour infusion (both on day 1 only), followed by 5-fluorouracil 750 mg/m^2 per day given as a 24-hour continuous infusion for 5 days, starting at the end of the cisplatin infusion. Treatment is repeated every three weeks. *Head and neck cancer:* Patients must receive premedication with antiemetics and appropriate hydration prior to and after. *Induction chemotherapy followed by radiotherapy (TAX 323):* for the induction treatment of inoperable locally advanced squamous cell carcinoma of the head and neck (SCCHN), the, the recommended dose of docetaxel is 75 mg/m^2 as a 1 hour infusion followed by cisplatin 75 mg/m^2 over 1 hour, on day one, followed by 5-fluorouracil as a continuous infusion at 750 mg/m^2 per day for five days. This regimen is administered every 3 weeks for 4 cycles. *Induction chemotherapy followed by chemoradiotherapy (TAX 324):* for the induction treatment of patients with locally advanced (technically unresectable, low probability of surgical cure, and aiming at organ preservation) squamous cell carcinoma of the head and neck (SCCHN) the recommended dose of docetaxel is 75 mg/m^2 as a 1 hour intravenous infusion on day 1, followed by cisplatin 100 mg/m^2 administered as a 30-minute to 3-hour infusion, followed by 5-fluorouracil 1000 mg/m^2/day as a continuous infusion from day 1 to day 4. This regimen is administered every 3 weeks for 3 cycles.

Contraindications: Hypersensitivity to the active substance or to any of the excipients; Patients with baseline neutrophil count of < 1,500 cells/mm^3; Patients with severe liver impairment. Contraindications for other medicinal products also apply when combined with docetaxel.

Warnings and Precautions: For breast and non-small cell lung cancers, premedication consisting of an oral corticosteroid, such as dexamethasone 16 mg per day (e.g. 8 mg twice daily) for 3 days starting 1 day prior to docetaxel administration, unless contraindicated, can reduce the incidence and severity of fluid retention as well as the severity of hypersensitivity reactions. For prostate cancer, the premedication is oral dexamethasone 8 mg, 12 hours, 3 hours and 1 hour before the docetaxel infusion. *Haematology:* Neutropenia is the most frequent adverse reaction of docetaxel. In the case of severe neutropenia (< 500 cells/mm^3 for seven days or more) during a course of docetaxel therapy, a reduction in dose for subsequent courses of therapy or the use of appropriate symptomatic measures are recommended. Patients receiving TCF and/or TAC should be closely monitored. *Gastrointestinal reactions:* Caution is recommended for patients with neutropenia, particularly at risk for developing gastrointestinal complications. Although majority of cases occurred during the first or second cycle of docetaxel containing regimen, enterocolitis could develop at any time, and could lead to death as early as on the first day of onset. *Hypersensitivity reactions:* Patients should be observed closely for hypersensitivity reactions, especially during the first and second infusions. Hypersensitivity reactions may occur within a few minutes following the initiation of the infusion of docetaxel, thus facilities for the treatment of hypotension and bronchospasm should be available. *Cutaneous reactions:* Localised skin erythema of the extremities (palms of the hands and soles of the feet) with oedema followed by desquamation has been observed. Severe symptoms such as eruptions followed by desquamation which lead to interruption or discontinuation of docetaxel treatment were reported. Severe Cutaneous Adverse Reactions (SCARs) such as Stevens-Johnson Syndrome (SJS), Toxic Epidermal Necrolysis (TEN) and Acute Generalised Exanthematous Pustulosis (AGEP) have been reported with docetaxel treatment. *Fluid retention:* Patients with severe fluid retention such as pleural effusion, pericardial effusion and ascites should be monitored closely. *Respiratory disorders:* Acute respiratory distress syndrome, interstitial pneumonia/pneumonitis, interstitial lung disease, pulmonary fibrosis and respiratory failure have been reported and may be associated with fatal outcome. Cases of radiation pneumonitis have been reported in patients receiving concomitant radiotherapy. *Nervous system:* The development of severe peripheral neurotoxicity requires a reduction of dose. *Cardiac toxicity:* Heart failure has been observed in patients receiving docetaxel in combination with trastuzumab, particularly following anthracycline (doxorubicin or epirubicin) - containing chemotherapy. Ventricular arrhythmia including ventricular tachycardia (sometimes

fatal) has been reported in patients treated with docetaxel in combination regimens including doxorubicin, 5-fluorouracil and/ or cyclophosphamide. Baseline cardiac assessment is recommended. *Eye disorders:* Cystoid macular oedema (CMO) has been reported in patients treated with docetaxel. *Second primary malignancies:* reported when docetaxel was given in combination with anticancer treatments known to be associated with second primary malignancies. *Tumour Lysis Syndrome:* reported with docetaxel after the first or the second cycle. *Other warnings:* The concomitant use of docetaxel with strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin and voriconazole) should be avoided. *Alcohol:* Docetaxel Accord concentrate contains alcohol. Harmful to those suffering from alcoholism. The amount of alcohol in this medicinal product and the side effects of the product may impair the ability to drive or use machines.

Fertility, Pregnancy & Lactation: *Women of childbearing potential/Contraception in males and females:* should be advised to avoid becoming pregnant, and to inform the treating physician immediately should this occur. An effective method of contraception should be used during treatment. Women of childbearing potential must use contraceptive measures during treatment and for 2 months after cessation of treatment with docetaxel. Men must use contraceptive measures during treatment and for 4 months after cessation of treatment with docetaxel. *Pregnancy:* must not be used during pregnancy unless clearly indicated. *Breast-feeding:* breast feeding must be discontinued for the duration of docetaxel therapy. *Fertility:* In non-clinical studies, docetaxel has genotoxic effects and may alter male fertility. Therefore, men being treated with docetaxel must seek advice on conservation of sperm prior to treatment.

Adverse Events include:
Adverse events which could be considered serious: Sepsis, Pneumonia, Neutropenia, Febrile neutropenia, Hypersensitivity, Peripheral neuropathy, Thrombocytopenia, Arrhythmia, Haemorrhage, Gastrointestinal haemorrhage, Cardiac failure, Neutropenic sepsis, Diabetes, Hypokalaemia, Neutropenic infection, Neurotoxicity, Myocardial ischaemia.

Other Very Common adverse events: Infections, Anaemia, Anorexia, Dysgeusia, Dyspnoea, Stomatitis, Diarrhoea, Nausea, Vomiting, Alopecia, Skin reaction, Nail disorders, Myalgia, Fluid retention, Asthenia, Pain, Fever, Insomnia, Paraesthesia, Headache, Hypoaesthesia, Lacrimation increased, Conjunctivitis, Lymphoedema, Epistaxis, Pharyngolaryngeal pain, Nasopharyngitis, Rhinorrhoea, Dyspepsia, Erythema, Rash, Pain in extremity, Bone pain, Back pain, Peripheral oedema, Pyrexia, Fatigue, Mucosal inflammation, Influenza-like illness, Chest pain, Chills, Weight increased, Decreased appetite, Hand-foot syndrome, Pharyngitis, Flatulence, Nail changes, Lethargy, Flu-like symptoms, Hot flush, Amenorrhoea, Parosmia, Oedema.

Other Common adverse events: Hypotension, Hypertension, Constipation, Abdominal pain, Arthralgia, Infusion site pain, Non-cardiac chest pain, Blood bilirubin increased, Blood alkaline phosphatase increased, Blood AST increased, Blood ALT increased, Oral candidiasis, Dehydration, Dizziness, Peripheral neuropathy, Upper abdominal pain, Dry mouth, Dermatitis, Rash erythematous, Nail discolouration, Onycholysis, Weight decreased, Cardiac left ventricular function disease, Exfoliative rash, Blurred vision, Hypocalcaemia, Hypophosphataemia, Phlebitis, Cough, Hearing impaired, Gastrointestinal pain, Odynophagia, Rash pruritus, Skin exfoliation, Cancer pain, Venous disorder, Oesophagitis, Dysphagia, Desquamation.

See SmPC for details of other adverse events.

Presentation and Price: 1 x 1ml vial: £145.80. 1 x 4ml vial: £479.06. 1 x 8ml vial: £958.11.

Legal Category: POM

Further information is available from: Accord-UK Ltd, Whiddon Valley, Barnstaple, Devon, EX32 8NS.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard
Adverse events should also be reported to Accord-UK LTD on 01271 385257 or email medinfo@accord-healthcare.com.

Accord-UK Ltd Electronic Certificate

Version: 2 . 0

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Document Name: UK Docetaxel Accord 20/1, 80/4, 160mg/8ml Concentrate Prescribing Information

Country: United Kingdom

Product: Docetaxel

Type: Material

Sub Type: Regulatory Material

Certification Statement

UK promotional item: I certify that I have examined the final form of the material and in my belief it is in accordance with the requirements of the relevant advertising regulations and the ABPI Code of Practice, is not inconsistent with the marketing authorisation and the summary of product characteristics and is a fair and truthful presentation of the facts about the medicine.

Meeting involving travel outside the UK: I certify that I have examined all the proposed arrangements for the meeting and that in my belief the arrangements are in accordance with the relevant advertising regulations and the ABPI Code of Practice.

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