AUROXEDA P1537881

AUROXEDA P1537881

PROFESSIONAL INFORMATION FOR HUMAN USE

SCHEDULING STATUS: S4

1. NAME OF MEDICINE

AUROXEDA 150 mg (film-coated tablet)

AUROXEDA 500 mg (film-coated tablet)

WARNING

Patients receiving concomitant capecitabine and oral coumarin-derivative anticoagulant therapy such as warfarin should have their anticoagulant response (INR or prothrombin time) monitored frequently in order to adjust the anticoagulant dose accordingly. A clinically important AUROXEDA-Warfarin interaction was demonstrated in a clinical pharmacology trial. Altered coagulation parameters and/or bleeding, including death, have been reported in patients taking AUROXEDA concomitantly with warfarin. Post-marketing reports have shown clinically significant increases in prothrombin time (PT) and INR in patients who were stabilised on anticoagulants at the time AUROXEDA was introduced. These events occurred within several days and up to several months after initiating AUROXEDA therapy and, in a few cases, within one month after stopping AUROXEDA. These events occurred in patients with and without liver metastases. Age greater than 60 and a diagnosis of cancer independently predispose patients to an increased risk of coagulopathy.

2. QUALITATIVE AND QUANTITIVE COMPOSITION:

AUROXEDA 150 mg:

Each film coated tablet contains capecitabine 150 mg. Contains sugar: 19,99 mg lactose.

AUROXEDA 500 mg:

Each film coated tablet contains capecitabine 500 mg. Contains sugar: 66,65 mg of lactose.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

AUROXEDA 150 mg:

Light peach coloured biconvex, oblong shaped film coated tablets, debossed with 150 on the one side and plain on the other side.

AUROXEDA 500 mg:

Peach coloured biconvex, oblong shaped film coated tablets, debossed with 500 on the one side and plain on the other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Breast Cancer

Metastatic breast cancer (Combination therapy): **AUROXEDA** in combination with docetaxel is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of cytotoxic chemotherapy which should have included an anthracycline.

Metastatic breast cancer (Monotherapy): **AUROXEDA** is indicated as monotherapy for the treatment of patients with locally advanced or metastatic breast cancer after failure of taxanes and an anthracycline-containing chemotherapy regimen or for whom further anthracycline therapy is not indicated.

Colorectal cancer

Colon cancer: **AUROXEDA** is indicated as adjuvant treatment after surgery, of patients with Dukes C colon cancer.

Metastatic colorectal cancer: **AUROXEDA** is indicated as treatment of patients with metastatic colorectal adenocarcinoma. The benefit relates to time to progression, while overall survival was not influenced.

Gastric Cancer: AUROXEDA is indicated as first line treatment of patients with advanced gastric adenocarcinoma in combination with other anti-chemotherapeutic regimen. The benefit relates to time to progression, while overall survival was not influenced.

4.2 Posology and method of administration

AUROXEDA should only be prescribed by a qualified medical practitioner experienced in the utilization of antineoplastic medicines. **AUROXEDA** tablets should be swallowed with water within 30 minutes after a meal. Treatment should be discontinued if progressive disease or intolerable toxicity is observed.

Adults

Monotherapy – Colon, colorectal and breast cancer

The recommended monotherapy dose of **AUROXEDA** is 1250 mg/m^2 administered twice daily (morning and evening: equivalent to 2 500 mg/m^2 total daily dose) for 14 days followed by a 7 day rest period.

Adjuvant treatment in patients with Stage III colon cancer is recommended for a maximum of six months.

Combination therapy

Colorectal and Gastric cancer: In combination treatment, the starting dose of **AUROXEDA should** be reduced to 1 000 mg/m^2 when administered twice daily for 14 days followed by a 7-day rest period. For the **AUROXEDA** Dose Reduction Schedule, please refer to Table 1. The inclusion of biological medicines in a combination regimen has no effect on the starting dose of **AUROXEDA.**

Premedication to maintain adequate hydration and anti-emesis according to the cisplatin prescribing information should be started prior to cisplatin administration for patients receiving the **AUROXEDA** plus cisplatin combination.

Breast Cancer: In combination with docetaxel for locally advanced or metastatic breast cancer, the recommended dose of **AUROXEDA** is 1 250 mg/m^2 twice daily for 14 days followed by a 7 day rest period, combined with docetaxel at 75 mg/m^2 as a 1 hour intravenous infusion every 3 weeks. Premedication with an oral corticosteroid such as dexamethasone, according to the docetaxel prescribing information, should be started prior to docetaxel administration for patients receiving the **AUROXEDA** plus docetaxel combination.

AUROXEDA dose is calculated according to body surface area.

Table 1: Standard and reduced dose calculations according to body surface area for a starting dose of **AUROXEDA** of 1250 mg/m^2

Table 1: Dose level 1 250 mg/m^2 (twice daily)					
Body Surface Area (m^2)	**Full dose 1 250 mg/m^2**	**Number of 150 mg tablets and/or 500 mg tablets per administration (each administration to be given morning and evening)**		**Reduced dose (75 %) 950 mg/m^2**	**Reduced dose (50 %) 625 mg/m^2**
	Dose per administration (mg)	**150 mg**	**500 mg**	**Dose per administration (mg)**	**Dose per administration (mg)**
≤ 1,26	1 500	-	3	1 150	800
1,27 – 1,38	1 650	1	3	1 300	800
1,39 – 1,52	1 800	2	3	1 450	950
1,53 – 1,66	2 000	-	4	1 500	1 000
1,67 – 1,78	2 150	1	4	1 650	1 000
1,79 – 1,92	2 300	2	4	1 800	1 150
1,93 – 2,06	2 500	-	5	1 950	1 300
2,07 – 2,18	2 650	1	5	2 000	1 300
≥ 2,19	2 800	2	5	2 150	1 450

Table 2: Standard and reduced dose calculations according to body surface area for a starting dose of **AUROXEDA** of 1 000 mg/m^2

Table 2: Dose level 1 000 mg/m^2 (twice daily)					
Body Surface Area (m^2)	**Full dose 1 000 mg/m^2**	**Number of 150 mg tablets and/or 500 mg tablets per administration (each administration to be given morning and evening)**		**Reduced dose (75 %) 750 mg/m^2**	**Reduced dose (50 %) 500 mg/m^2**
	Dose per administration (mg)	**150 mg**	**500 mg**	**Dose per administration (mg)**	**Dose per administration (mg)**
≤ 1,26	1 150	1	2	800	600
1,27 – 1,38	1 300	2	2	1 000	600
1,39 – 1,52	1 450	3	2	1 100	750
1,53 – 1,66	1 600	4	2	1 200	800
1,67 – 1,78	1 750	5	2	1 300	800
1,79 – 1,92	1 800	2	3	1 400	900
1,93 – 2,06	2 000	-	4	1 500	1 000
2,07 – 2,18	2 150	1	4	1 600	1 050
≥ 2,19	2 300	2	4	1 750	1 100

Dose adjustments during treatment

Patients should be carefully monitored for toxicity. Toxicity due to **AUROXEDA** administration may be managed by symptomatic treatment and/or modification of the **AUROXEDA** dose (treatment interruption or dose reduction).

Dosage modifications are not recommended for Grade 1 events. Therapy with **AUROXEDA** should be interrupted upon the occurrence of a Grade 2 or 3 adverse experiences. Once the adverse event has resolved or decreased in intensity to Grade 1, then **AUROXEDA** therapy may be restarted at full dose or adjusted according to the table below. If a Grade 4 experience occurs, therapy should be discontinued or interrupted until resolved or decreased to Grade 1, and therapy can then be restarted at 50 % of the original dose.

Patients taking **AUROXEDA** should be informed of the need to interrupt treatment immediately if moderate or worse toxicity occurs.

Doses of **AUROXEDA** omitted for toxicity are not replaced or restored; instead the patient should resume the planned treatment cycles. Once the dose has been reduced it should not be increased at a later time. See section 4.4 and 4.8. The following table shows the recommended dose modifications following toxicity with **AUROXEDA.**

Table 3: AUROXEDA Dose Reduction Schedule following toxicity (3-weekly cycle or continuous treatment)

Toxicity NCIC Grades*	**Dose changes within a treatment cycle**	**Dose adjustment for next cycle/dose (% of starting dose)**
• ***Grade 1***	Maintain dose level	Maintain dose level
• ***Grade 2***		
1st appearance	Interrupt until resolved to Grade 0 – 1	100 %
2nd appearance	Interrupt until resolved to Grade 0 – 1	75 %
3rd appearance	Interrupt until resolved to Grade 0 – 1	50 %
4th appearance	Discontinue treatment permanently	
• ***Grade 3***		
1st appearance	Interrupt until resolved to Grade 0 – 1	75 %
2nd appearance	Interrupt until resolved to Grade 0 – 1	50 %
3rd appearance	Discontinue treatment permanently	
• ***Grade 4***		
1st appearance	Discontinue permanently or if medical practitioner deems it to be in the patient's best interest to continue, interrupt until resolved to Grade 0 - 1	50 %
2nd appearance	Discontinue treatment permanently	

* According to the National Cancer Institute of Canada Clinical Trial Group

(NCIC CTG) Common Toxicity Criteria (version 1) or the Common Terminology Criteria for Adverse Events (CTCAE) of the Cancer Therapy Evaluation Program, US National Cancer Institute, version 3.0.

For hand-foot syndrome and hyperbilirubinaemia, see section 4.4 and 4.8.

Haematology: Patients with baseline neutrophil counts of ≤ 1,5 x 10^9/L and/or thrombocyte counts of < 100 x 10^9/L should not be treated with the **AUROXEDA.** If unscheduled laboratory assessments during a treatment cycle show Grade 3 or 4 haematologic toxicity, treatment with **AUROXEDA** should be interrupted.

Dose modifications for toxicity when AUROXEDA is used as a 3 weekly cycle in combination with other medicines:

Dose modifications for toxicity when **AUROXEDA** is used as a 3 week cycle in combination with other medicines should be made according to Table 3 above for **AUROXEDA** and according to the appropriate prescribing information for the other-medicine(s).

At the beginning of a treatment cycle, if a treatment delay is indicated for either **AUROXEDA** or the other medicine(s), then administration of all medicines should be delayed until the requirements for restarting all medicines are met.

During a treatment cycle for those toxicities considered by the treating medical practitioner not to be related to **AUROXEDA**, **AUROXEDA** should be continued and the dose of the other medicine(s) should be adjusted according to the appropriate prescribing information. If other medicines have to be discontinued permanently, **AUROXEDA** treatment can be resumed when the requirements for restarting are met. This advice is applicable to all indications and to all special populations.

Dose modifications for toxicity when AUROXEDA is used continuously in combination with other medicines:

Dose modifications for toxicity when **AUROXEDA** is used continuously in combination with other medicine(s) should be made according to Table 3 above for **AUROXEDA** and according to the appropriate prescribing information for the other medicine(s).

Dosing in special populations

Patients with hepatic-impairment due to liver metastases: In patients with mild to moderate hepatic impairment due to liver metastases, no starting dose adjustment is necessary. However, such patients should be carefully monitored. Patients with severe hepatic impairment have not been studied. (See sections 4.3 and 4.4).

Patients with renal impairment: **AUROXEDA** is contra-indicated in patients with severe renal impairment (creatinine clearance below 30 ml/min). (See section 4.3). The incidence of Grade 3 or 4 adverse reactions in patients with moderate renal impairment (creatinine clearance 30 – 50 ml/min at baseline) is increased compared to the overall population.

In patients with moderate renal impairment (creatinine clearance 30 – 50 ml/min) at baseline, a dose reduction to 75 % for starting dose of 1 250 mg/m^2 is recommended. In patients with moderate renal impairment at baseline, no dose reduction is required for a starting dose of 1 000 mg/m^2. In patients with mild renal impairment (creatinine clearance 51 – 80 mg/min), no adjustment in starting dose is recommended. Careful monitoring and prompt treatment interruption is recommended if the patient develops a Grade 2, 3 or 4 adverse event, with subsequent dose adjustment as outlined in the table above. The dose adjustment recommendation for patients with moderate renal impairment apply both to monotherapy and combination use. (See section 4.8 and 5.2)

Children: Safety and efficacy in children have not been established.

Elderly: No adjustment of the starting dose is needed for **AUROXEDA** monotherapy. However, severe Grade 3 or 4 treatment-related and adverse events were more frequent in patients over 60 years of age compared to younger patients, Careful monitoring of elderly patients is advisable. For treatment with **AUROXEDA**:

- In combination with docetaxel, an increased incidence of Grade 3 or 4 treatment-related adverse reactions and treatment-related serious adverse reactions were reported in patients 60 years of age or more. For patients 60 years of age or more treated with the combination of **AUROXEDA** plus docetaxel, a starting dose reduction of **AUROXEDA** to 75 % (950 mg/m^2 twice daily) is recommended. If no toxicity is reported in patients ≥ 60 years of age treated with a reduced **AUROXEDA** starting dose in combination with docetaxel, the dose of **AUROXEDA** may be cautiously escalated to 1 250 mg/m^2 twice daily.
- In combination with irinotecan: for patients 65 years of age or more treated with the combination of **AUROXEDA** with irinotecan, a starting dose reduction of **AUROXEDA** to 800 mg/m^2 twice daily is recommended.

4.3 Contraindications

AUROXEDA is contraindicated in:

- patients with known hypersensitivity to capecitabine or to any of its components.
- patients who have a history of severe and unexpected reactions to fluoropyrimidine therapy, or with known hypersensitivity to fluorouracil (capecitabine metabolite).
- patients with known dihydropyrimidine dehydrogenase (DPD) deficiency.
- patients with severe leukopaenia, neutropenia, or thrombocytopenia.
- patients with severe hepatic impairment.
- in patients with severe renal impairment (creatinine clearance below 30 ml/min).
- Pregnancy and breastfeeding (see section 4.6).

AUROXEDA should not be administered with sorivudine or its chemically related analogues, such as brivudine. (See section 4.5). If contra-indications exist for any of the medicines in the combination regimen, that medicine should not be used.

4.4 Special warnings and precautions for use

Coagulopathy

Patients receiving concomitant capecitabine and oral coumarin-derivative anticoagulant therapy should have their anticoagulant response (INR or prothrombin time) monitored closely with great frequency and the anticoagulant dose should be adjusted accordingly (see boxed warning and section 4.5).

Diarrhoea

Capecitabine can induce diarrhoea, sometimes severe. Patients with severe diarrhoea should be carefully monitored and given fluid and electrolyte replacement if they become dehydrated. In 875 patients with either metastatic breast or colorectal cancer who received capecitabine monotherapy, the median time to first occurrence of Grade 2 to 4 diarrhoea was 34 days (range from 1 to 369 days). The median duration of Grade 3 to 4 diarrhoea was 5 days. National Cancer Institute of Canada (NCIC) Grade 2 diarrhoea is defined as an increase of 4 to 6 stools/day or nocturnal stools, Grade 3 diarrhoea as an increase of 7 to 9 stools/day or incontinence and malabsorption, and Grade 4 diarrhoea as an increase of ≥10 stools/day or grossly bloody diarrhoea or the need for parenteral support. If Grade 2, 3 or 4 diarrhoea occurs, administration of capecitabine should be immediately interrupted until the diarrhoea resolves or decreases in intensity to Grade 1 (see section 4.2). Standard antidiarrhoeal treatments (e.g. loperamide) are recommended. (See section 4.8). Necrotising enterocolitis (typhlitis) has been reported.

Cardiotoxicity

The cardiotoxicity observed with capecitabine includes myocardial infarction/ischemia, angina, dysrhythmias, cardiac arrest, cardiac failure, sudden death, electrocardiographic changes, and cardiomyopathy. These adverse reactions may be more common in patients with a prior history of coronary artery disease.

Dihydropyrimidine Dehydrogenase Deficiency

Patients with certain homozygous or certain compound heterozygous mutations in the DPD gene that result in complete or near complete absence of DPD activity are at increased risk for acute early-onset of toxicity and severe, life-threatening, or fatal adverse reactions caused by capecitabine (e.g., mucositis, diarrhoea, neutropenia, and neurotoxicity). Patients with partial DPD activity (see section 4.3) may also have increased risk of severe, life-threatening, or fatal adverse reactions caused by capecitabine.

Withhold or permanently discontinue capecitabine based on clinical assessment of the onset, duration and severity of the observed toxicities in patients with evidence of acute early-onset or unusually severe toxicity, which may indicate near complete or total absence of DPD activity. No capecitabine dose has been proven safe for patients with complete absence of DPD activity. There is insufficient data to recommend a specific dose in patients with partial DPD activity as measured by any specific test.

Dehydration and Renal Failure

Dehydration has been observed and may cause acute renal failure which can be fatal. Patients with pre-existing compromised renal function or who are receiving concomitant capecitabine with known nephrotoxic medicines are at higher risk. Patients with anorexia, asthenia, nausea, vomiting or diarrhoea may rapidly become dehydrated. Monitor patients when capecitabine is administered to prevent and correct dehydration at the onset. If Grade 2 (or higher) dehydration occurs, capecitabine treatment should be immediately interrupted and the dehydration corrected. Treatment should not be restarted until the patient is rehydrated and any precipitating causes have been corrected or controlled. Dose modifications should be applied for the precipitating adverse event as necessary (see section 4.2).

Patients with moderate renal impairment at baseline require dose reduction (see section 4.2 and 5.2). Patients with mild and moderate renal impairment at baseline should be carefully monitored for adverse reactions. Prompt interruption of therapy with subsequent dose adjustments is recommended if a patient develops a Grade 2 to 4 adverse event as outlined in Table 2 (see section 4.2 and 5.2).

Mucocutaneous and Dermatologic Toxicity

Severe mucocutaneous reactions, some with fatal outcome, such as Stevens-Johnson syndrome and Toxic Epidermal Necrolysis (TEN) can occur in patients treated with capecitabine (see section 4.8). Capecitabine should be permanently discontinued in patients who experience a severe mucocutaneous reaction possibly attributable to capecitabine treatment.

Hand-and-foot syndrome (palmar-plantar erythrodysesthesia or chemotherapy-induced acral erythema) is a cutaneous toxicity. Median time to onset was 79 days (range from 11 to 360 days) with a severity range of Grades 1 to 3 for patients receiving capecitabine monotherapy in the metastatic setting. Grade 1 is characterized by any of the following: numbness, dysesthesia/paresthesia, tingling, painless swelling or erythema of the hands and/or feet and/or discomfort which does not disrupt normal activities. Grade 2 hand-and-foot syndrome is defined as painful erythema and swelling of the hands and/or feet and/or discomfort affecting the patient's activities of daily living. Grade 3 hand-and-foot syndrome is defined as moist desquamation, ulceration, blistering or severe pain of the hands and/or feet and/or severe discomfort that causes the patient to be unable to work or perform activities of daily living. Persistent or severe hand-and-foot syndrome (Grade 2 and above) can eventually lead to loss of fingerprints which could impact patient identification. If Grade 2 or 3 hand-and-foot syndrome occurs, administration of capecitabine should be interrupted until the event resolves or decreases in intensity to Grade 1. Following Grade 3 hand-and-foot syndrome, subsequent doses of capecitabine should be decreased (see section 4.2).

Hyperbilirubinemia

If medicine-related Grade 3 to 4 elevations in bilirubin, or medicine related elevations in hepatic aminotransferases (ALT, AST) occur, administration of capecitabine should be immediately interrupted until the hyperbilirubinemia decreases to ≤ 3,0 x ULN or hepatic aminotransferases decreases to ≤ 2,5 x ULN. (see recommended dose modifications under section 4.2).

Haematologic

Patients with baseline neutrophil counts of < 1,5 x 10^9/L and/or thrombocyte counts of < 100 x 10^9/L should not be treated with **AUROXEDA**. If unscheduled laboratory assessments during a treatment cycle show Grade 3 or 4 hematologic toxicity, treatment with capecitabine should be interrupted. (See section 4.2)

Elderly Patients

Patients ≥ 80 years old may experience a greater incidence of Grade 3 or 4 adverse reactions.

Hepatic Insufficiency

Patients with mild to moderate hepatic dysfunction due to liver metastases should be carefully monitored when capecitabine is administered. The effect of severe hepatic dysfunction on the disposition of capecitabine is not known (see section 4.3 and 5.2).

Paediatric Use

The safety and effectiveness of **AUROXEDA** in paediatric patients has not been established.

Lactose:

As this medicinal product contains anhydrous lactose as an excipient, patients with rare hereditary problems of galactose intolerance, Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

Anticoagulants

Altered coagulation parameters and/or bleeding have been reported in patients taking **AUROXEDA** concomitantly with coumarin-derivative anticoagulants such as warfarin and phenprocoumon [see Boxed Warning]. In a medicine interaction study with single-dose warfarin administration, there was a significant increase in the mean AUC of S-warfarin (see section 5.2). The maximum observed INR value increased by 91 %. This interaction is probably due to an inhibition of cytochrome P450 2C9 by capecitabine and/or its metabolites.

Sorivudine and analogues

A clinically significant interaction between sorivudine and 5-FU, resulting from the inhibition of dihydropyrimidine dehydrogenase by sorivudine, has been described in the literature. This interaction, which leads to increased fluoropyrimide toxicity is potentially fatal. Therefore, **AUROXEDA** should not be administered with sirovudine or its chemically related analogues such as brivudine. (See section 4.3)

Phenytoin

The level of phenytoin should be carefully monitored in patients taking **AUROXEDA** and phenytoin dose may need to be reduced. Postmarketing reports indicate that some patients receiving **AUROXEDA** and phenytoin had toxicity associated with elevated phenytoin levels. Formal medicine interaction studies with phenytoin have not been conducted, but the mechanism of interaction is presumed to be inhibition of the CYP2C9 isoenzyme by **AUROXEDA** and/or its metabolites.

Leucovorin

The concentration of 5-fluorouracil is increased and its toxicity may be enhanced by leucovorin. Deaths from severe enterocolitis, diarrhoea, and dehydration have been reported in elderly patients receiving weekly leucovorin and fluorouracil.

CYP2C9 substrates

Other than warfarin, no formal medicine interaction studies between **AUROXEDA** and other CYP2C9 substrates have been conducted. Care should be exercised when **AUROXEDA** is coadministered with CYP2C9 substrates.

Allopurinol

Concomitant use with allopurinol may decrease concentration of **AUROXEDA** active metabolites (see section 5.2), which may decrease **AUROXEDA** efficacy. Avoid the use of allopurinol during treatment with **AUROXEDA**.

Interferon Alpha

The maximum tolerated dose (MTD) of capecitabine alone using the intermittent regimen is 3000 mg/m^2 per day whereas it is only 2000 mg/m^2 per day when **AUROXEDA** was combined with interferon alpha-2a (3MIU/m^2 per day) compared to 3000 mg/m^2 when **AUROXEDA** was used alone.

Antacids

The effect of an aluminium hydroxide and magnesium hydroxide-containing antacid on the pharmacokinetics of capecitabine was investigated. There was a small increase in plasma concentrations of capecitabine and one metabolite (5'-DFCR); there was no effect on the 3 major metabolites (5'-DFUR, 5-FU and FBAL).

Radiotherapy

The MTD of capecitabine alone using the intermittent regimen is 3000 mg/m^2 per day, whereas, when combined with radiotherapy for rectal cancer, the MTD of capecitabine is 2000 mg/m^2 per day using either a continuous schedule or given daily Monday through Friday during a 6-week course of radiotherapy.

Oxaliplatin

No clinically significant differences in exposure to capecitabine or its metabolites, free platinum or total platinum occurred when capecitabine was administered in combination with oxaliplatin or in combination with oxaliplatin and bevacizumab.

Bevacizumab

There was no clinically significant effect of bevacizumab on the pharmacokinetic parameters of capecitabine or its metabolites in the presence of oxaliplatin.

Food Interaction

Food was shown to reduce both the rate and extent of absorption of **AUROXEDA** (see section 5.2). In all clinical trials, patients were instructed to administer **AUROXEDA** within 30 minutes after a meal. It is recommended that **AUROXEDA** be administered with food (see section 4.2).

4.6 Fertility, pregnancy and lactation

Pregnancy

AUROXEDA is contraindicated during pregnancy (see section 4.3).

Based on findings in animal reproduction studies and its mechanism of action, **AUROXEDA** can cause foetal harm when administered to a pregnant woman (see section 5.2). Limited available human data are not sufficient to inform the medicine-associated risk during pregnancy. In animal reproduction studies, administration of **AUROXEDA** to pregnant animals during the period of organogenesis caused embryo lethality and teratogenicity in mice and embryo lethality in monkeys at 0,2 and 0,6 times the exposure (AUC) in patients receiving the recommended dose respectively (see section 5.3). Advise pregnant women of the potential risk to a foetus.

Lactation

There is no information regarding the presence of **AUROXEDA** in human milk, or on its effects on milk production or the breast-fed infant. Capecitabine metabolites were present in the milk of lactating mice [see Data]. Because of the potential for serious adverse reactions from capecitabine exposure in breast-fed infants, advise women not to breastfeed during treatment with **AUROXEDA** and for 2 weeks after the final dose. (See section 4.3)

DETACH BEFORE DISPENSING

PATIENT INFORMATION LEAFLET

S4

AUROXEDA 150 mg (film coated tablet)

AUROXEDA 500 mg (film coated tablet)

Capecitabine

(Contains sugar: lactose monohydrate)

Read all of this leaflet carefully before you start taking AUROXEDA.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **AUROXEDA** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What **AUROXEDA** is and what it is used for
2. What you need to know before you take **AUROXEDA**
3. How to take **AUROXEDA**
4. Possible side effects
5. How to store **AUROXEDA**
6. Contents of the pack and other information

1. WHAT AUROXEDA IS AND WHAT IS USED FOR

AUROXEDA contain a medicine called capecitabine.

This belongs to a class of cytostatic medicines (medicines that inhibits cell growth).

AUROXEDA used in the treatment of cancers especially breast cancer, colorectal cancer and gastric cancer.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE AUROXEDA

Do not take AUROXEDA:

- If you have ever had an allergic reaction to **AUROXEDA** or any ingredient of the **AUROXEDA**.
- If you have a history of severe unexpected reactions with fluoropyrimidine therapy (this is also an anticancer medicine).
- If you have ever had any hypersensitivity reactions to fluorouracil (capecitabine metabolite).
- If you are dihydropyrimidine dehydrogenase deficient (DPD is a certain type of metabolic disorder).
- If you have any type of blood disorder like leukopaenia (abnormal lowering of the white blood cell count), neutropenia [abnormally low concentration of neutrophils (a type of white blood cell)], or thrombocytopenia (a condition in which you have a low blood platelet count).
- If you have severe liver problems.
- If you have severe kidney problems.
- If you are being treated with sorivudine now or in the last 4 weeks or its analogues like brivudine (these are antiviral medicines).
- If you are pregnant or planning to become pregnant or breastfeeding.

Warnings and precautions

Take special care with **AUROXEDA** by telling your doctor**:**

- If you are taking blood thinning medicine such as warfarin.
- If you have diarrhoea.
- If you are or become dehydrated because of severe nausea and vomiting.
- If you have heart problems.
- If you have liver problems.
- If you have kidney problems.
- If you have numbness and changes in sensation, redness, pain or swelling of your hands and feet as **AUROXEDA** can also cause "hand and foot syndrome".

Taking other medicines with AUROXEDA:

Always tell your healthcare professional if you are taking any other medicine (This includes complementary and traditional medicines).

AUROXEDA may have an effect on other medicines or other medicines may have an effect on **AUROXEDA**.

- Blood clotting and bleeding parameters may be changed when **AUROXEDA** is given with warfarin or phenoprocoumon.
- Phenytoin plasma concentrations and toxicity symptoms are increased when **AUROXEDA** is given with phenytoin (used to treat epilepsy).
- Plasma concentration of **AUROXEDA** is increased when **AUROXEDA** is given with antacids (antacids are medicines which neutralises the stomach acidity).
- Dose should be reduced when **AUROXEDA** is given with folinic acid (decrease the toxic effects of methotrexate and pyrimethamine) or interferon alfa (medicine used to treat viral infections and cancers).
- If you are currently being treated or have had a previous history with radiotherapy, you may be more likely to experiencing side effects.
- A possible life-threatening interaction exists between **AUROXEDA** and sirovudine or its chemically related analogues such as brivudine therefore these medicines should not be administered together.

Taking AUROXEDA with food and drink:

AUROXEDA should be swallowed with water within 30 minutes after a meal.

Pregnancy and breastfeeding:

If you are pregnant or breastfeeding your baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking **AUROXEDA.**

AUROXEDA is not recommended during pregnancy or breastfeeding, (see 'Do not take **AUROXEDA**') as **AUROXEDA** may be harmful to the baby.

Both men and women must ensure adequate birth control measures are taken whilst receiving **AUROXEDA**. Your doctor will advise you on the contraception method to be used and duration of contraception use. Contraception is typically used for 3 months after completing treatment with **AUROXEDA** in men and 6-12 months after completing treatment with **AUROXEDA** in women.

Driving and using machinery:

Since **AUROXEDA** may cause dizziness (a feeling that you are about to fall), tiredness and vision problems, this may influence your ability to drive, use machinery or perform any other tasks that require concentration.

AUROXEDA contains lactose:

AUROXEDA contains lactose, which is a type of sugar. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. HOW TO TAKE AUROXEDA

Do not share medicines prescribed for you with any other person.

Always take **AUROXEDA** exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure.

The recommended dose may vary depending on the type and severity of your cancer, your age and your body surface area.

AUROXEDA should be swallowed with a glass of water within 30 minutes after a meal.

Your doctor will tell you how long your treatment with **AUROXEDA** will last. Do not stop treatment early because this may cause reoccurrence of your condition. If you have the impression that the effect of **AUROXEDA** is too strong or too weak, tell your doctor or pharmacist.

If you take more AUROXEDA than you should:

If you take more than your required dose you may experience nausea, vomiting, diarrhoea (frequent and watery bowel movements), mucositis (inflammation of mucous membrane), gastrointestinal irritation, bleeding and bone marrow depression.

Symptomatic and supportive measures should be provided.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take AUROXEDA:

If you forget to take a dose, take it as soon as you remember unless it is nearly time for your next dose. Do not take a double dose to make up for forgotten individual doses.

4. POSSIBILE SIDE EFFECTS

Not all side effects reported for **AUROXEDA** are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking this medicine, please consult your doctor, pharmacist or other health care professional for advice.

AUROXEDA can have side effects:

If any of the following happens, stop taking **AUROXEDA** and tell your doctor immediately or go to the casualty department at your nearest hospital:

- Swelling of the hands, feet, ankles, face, lips, mouth and throat, which may cause difficulty in breathing,
- pruritus (an intense itching sensation),
- skin discoloration,
- skin ulceration or blistering of the skin, mouth, eyes or genitals as this may be due to a serious allergic reaction known as Stevens-Johnson Syndrome.

These are all very serious side effects. If you have them, you may have had a serious allergic reaction to **AUROXEDA**. You may need urgent medical attention or hospitalisation.

Tell your doctor if you notice any of the following:

Frequent side effects:

- decreases in the amount of red blood cells, white blood cells and platelets (seen in blood tests),
- loss of appetite,
- abdominal or stomach pain,
- diarrhoea (frequent and watery bowel movements) moderate or severe,
- stomatitis (sores in mouth and throat),
- constipation (difficult evacuation of the bowels) mild or moderate,
- nausea,
- unusual tiredness,
- vomiting,
- hyperbilirubinaemia (high amounts of bile pigment (bilirubin) in the blood),
- dermatitis (inflammation of the skin),
- hand and foot syndrome (redness, swelling, and pain on the palms of the hands and/or the soles of the feet).

Less frequent side effects:

- encephalopathy (brain related disease or disorder),
- fungal infection,
- infection,
- keratoconjunctivitis (inflammation of the cornea and conjunctiva),
- sepsis (presence of pus-forming bacteria or their toxins in the blood or tissues),
- viral infection,
- influenza like illness,
- irritability,
- coagulation disorder (blood clotting disorder),
- leukopenia (abnormal lowering of the white blood cell count),
- lymphedema (lymph accumulating in the tissues),
- hypokalemia (low level of potassium in the circulating blood),
- hypomagnesemia (lower serum magnesium concentration),
- hypertriglyceridemia (higher blood levels of triglycerides),
- dehydration (depletion of bodily fluids),
- loss of consciousness,
- dizziness (a feeling that you are about to fall),
- insomnia (chronic sleeplessness),
- confusion,
- depression,
- ataxia (inability to coordinate voluntary muscle movements),
- headache,
- paresthesia (abnormal skin sensations),
- impaired balance,
- tremor (involuntary vibration),
- conjunctivitis (inflammation of the conjunctiva of the eye),
- eye irritation,
- angina pectoris - (heart condition marked by chest pain),
- atrial fibrillation,
- bradycardia (abnormally slow heartbeat),
- cardiomyopathy (heart muscle disorder),
- cardiotoxicity (damage to the heart muscle),
- extrasystoles (a heartbeat outside the normal rhythm),
- myocarditis (inflammation of the myocardia of the heart),
- pericardial effusion (fluid around the heart),
- tachycardia (abnormally higher heart beat),
- ventricular extrasystoles (extra, abnormal heartbeats that begin in one of ventricles),
- cerebrovascular accident,
- hypotension (abnormally low blood pressure),
- hypertension (abnormally high blood pressure),
- phlebitis (inflammation of a vein (usually in the legs)),
- thrombophlebitis (conjunction with the formation of a blood clot),
- deep vein thrombosis,
- hot flushes (sudden brief sensation of heat),
- bronchitis (inflammation of bronchus),
- bronchopneumonia (acute inflammation of the walls of the bronchioles),
- bronchospasm (spasm of the bronchi that makes exhalation difficult and noisy),
- dyspnea (difficult or laboured respiration),
- respiratory distress,
- dysarthria (impaired speech ability),
- epistaxis (bleeding from the nostril, nasal cavity, or nasopharynx),
- hemoptysis (coughing up of blood or blood-stained mucus from the bronchi, larynx, trachea, or lungs),
- pneumonia (inflammation of the lung parenchyma),
- pulmonary embolism (blockage of the pulmonary artery),
- asthma (inflammation and narrowing of the airways),
- cough,
- hoarseness (a throaty harshness),
- laryngitis (inflammation of larynx),
- dysphasia (language disorder marked by deficiency in the generation of speech),
- gastric ulcer,
- gastrointestinal hemorrhage (bleeding in the gastrointestinal tract),
- gastrointestinal tract toxicity,
- hemorrhage (bleeding),
- ileus (blockage of the intestine (especially the ileum)),
- dyspepsia (digestive function disorder),
- abdominal distension (air (gas) or fluid, accumulate in the abdomen),
- abnormal coordination,
- ascites (accumulation of serous fluid in peritoneal cavity),
- gastroenteritis (inflammation of the stomach and intestines),
- gastrointestinal mobility disorder,
- cholestatic hepatitis (blockage of the bile ducts outside of the liver),
- hepatic fibrosis or hepatitis (inflammation of the liver),
- photosensitivity (sensitivity to light),
- radiation recall syndrome (severe skin reaction that occurs when certain chemotherapy drugs are administered during or soon after radiation treatment),
- nail disorder,
- sweating increased,
- bone marrow depression,
- arthralgia (pain in a joint),
- back pain,
- arthritis (Inflammation of one or more joints),
- bone pain,
- difficulty in walking,
- fibrosis (development of excess fibrous connective tissue in an organ),
- muscle weakness,
- renal impairment (kidney problems),
- proctalgia (condition in which the kidneys lose the ability to remove waste and balance fluids),
- collapse,
- fever,
- pyrexia (raised body temperature – fever),
- thirst (a feeling of needing or wanting to drink something),
- increased weight.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects to SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: http:///www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of **AUROXEDA.**

5. HOW TO STORE AUROXEDA

Store at or below 30 °C.

Keep the blisters in the carton until required for use.

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What AUROXEDA contains

The active substance is capecitabine.

AUROXEDA 150 mg:

Each film coated tablet contains capecitabine 150 mg. Contains sugar: 19,99 mg lactose.

AUROXEDA 500 mg:

Each film coated tablet contains capecitabine 500 mg. Contains sugar: 66,65 mg of lactose.

The other ingredients of **AUROXEDA** are cellulose microcrystalline, croscarmellose sodium, ferric oxide red, ferric oxide yellow, hypromellose, magnesium stearate, talc and titanium dioxide.

What AUROXEDA looks like and contents of the pack

AUROXEDA 150 mg:

Light peach coloured biconvex, oblong shaped film coated tablets, debossed with 150 on the one side and plain on the other side.

AUROXEDA 500 mg:

Peach coloured biconvex, oblong shaped film coated tablets, debossed with 500 on the one side and plain on the other side.

Blister pack:

Tablets are packed in clear 250 micrometer PVC film coated with 90 g/m^2 PVdC as the forming material and 25 micrometer aluminium foil with 7 g/m^2 heat seal lacquer as the lidding material.

For 150 mg:

Pack size: 60s – Each carton contains 6 blisters of 10 tablets each.

For 500 mg:

Pack size: 120s – Each carton contains 12 blisters of 10 tablets each.

Holder of Registration

Aurogen South Africa (Pty) Ltd
Woodhill Office Park, Building 1, First Floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

This leaflet was revised in

21 August 2024

Registration number:

AUROXEDA 150 mg: 53/26/0100

AUROXEDA 500 mg: 53/26/0101

Fertility

Pregnancy Testing

Pregnancy testing is recommended for females of reproductive potential prior to initiating **AUROXEDA**.

Contraception

Females

AUROXEDA can cause fetal harm when administered to a pregnant woman. Advise females of reproductive potential to use effective contraception during treatment and for 6 months following the final dose of **AUROXEDA**. The recommended duration of contraception in female patients should be until the end of relevant systemic exposure to the genotoxic compound including potential genotoxic metabolites (i.e. five half-lives after the last dose) plus 6 months. The duration of folliculogenesis is described as 6 to 12 months. The 6-month contraception recommendation for genotoxic pharmaceuticals after cessation of therapy covers the growth and maturation phase of folliculogenesis and is expected to allow elimination of most damaged follicles and oocytes.

Males

Based on genetic toxicity findings, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months following the last dose of **AUROXEDA**.

The recommended duration of contraception in male patients should be until the end of relevant systemic exposure to the genotoxic compound incl. potential genotoxic metabolites (i.e. five half-lives after the last dose) plus 90 days. Use of contraception for a period of 3 months after cessation of therapy will minimize the risk of adverse embryo-fetal effects from genotoxic pharmaceuticals. The lower limit of the period of spermatogenesis and the epididymal maturation.

Infertility

Based on animal studies, **AUROXEDA** may impair fertility in females and males of reproductive potential.

4.7 Effects on ability to drive and use machines

AUROXEDA has minor or moderate influence on the ability to drive and use machines. **AUROXEDA** may cause dizziness, fatigue and nausea.

4.8 Undesirable Effects

a. Summary of the safety profile

The overall safety profile of **AUROXEDA** is based on data from over 3000 patients treated with **AUROXEDA** as monotherapy or capecitabine in combination with different chemotherapy regimens in multiple indications. The safety profiles of **AUROXEDA monotherapy** for the metastatic breast cancer, metastatic colorectal cancer and adjuvant colon cancer populations are comparable.

The most commonly reported and/or clinically relevant treatment-related adverse drug reactions (ADRs) were gastrointestinal disorders (especially diarrhoea, nausea, vomiting, abdominal pain, stomatitis), hand-foot syndrome (palmar-plantar erythrodysesthesia), fatigue, asthenia, anorexia, cardiotoxicity, increased renal dysfunction on those with preexisting compromised renal function, and thrombosis/embolism.

b. Tabulated list of adverse reactions

ADRs considered by the investigator to be possibly, probably, or remotely related to the administration of capecitabine are listed in Table 4 for capecitabine given as monotherapy and in Table 5 for capecitabine given in combination with different chemotherapy regimens in multiple indications. The following headings are used to rank the ADRs by frequency. Within each frequency grouping, ADRs are presented in order of decreasing seriousness.

Capecitabine Monotherapy:

Table 4 lists ADRs associated with the use of capecitabine monotherapy based on a pooled analysis of safety data from three major studies.

Table 4 Summary of related ADRs reported in patients treated with capecitabine monotherapy

Body System	*Frequent All Grades*	*Less frequent Severe and/or Life-threatening (Grade 3-4) or considered medically relevant*	*Frequency unknown (Post-Marketing Experience)*
Infections and infestations	Herpes viral infection, Nasopharyngitis, Lower respiratory tract infection	Sepsis, Urinary tract infection, Cellulitis, Tonsillitis, Pharyngitis, Oral candidiasis, Influenza, Gastroenteritis, Fungal infection, Herpes Infection, Tooth abscess	
Neoplasm benign, malignant and unspecified		Lipoma	
Blood and lymphatic system disorders	Neutropenia, Anaemia	Febrile neutropenia, Pancytopenia, Granulocytopenia, Thrombocytopenia, Leukopenia, Haemolytic anaemia, International Normalised Ratio (INR) increased*Prothrombin time prolonged	
Immune system disorders		Hypersensitivity	
Metabolism and nutrition disorders	Anorexia Dehydration, Weight decreased	Diabetes, Hypokalaemia, Appetite disorder, Malnutrition, Hypertriglyceridaemia	
Psychiatric disorders		Confusional state, Panic attack, Depressed mood, Libido decreased	
Nervous system disorders	Headache, Lethargy Dizziness, Parasthesia Dysgeusia	Aphasia, Memory impairment, Ataxia, Syncope, Balance disorder, Sensory disorder, Neuropathy peripheral	Toxic leukoencephalopathy (very rare)
Eye disorders	Lacrimation increased, Conjunctivitis, Eye irritation	Visual acuity reduced, Diplopia	Lacrimal duct stenosis (rare), Comeal disorders(rare), keratitis (rare), punctate keratitis (rare)
Ear and labyrinth disorders		Vertigo, Ear pain	
Cardiac disorders		Angina unstable, Angina pectoris, Myocardial ischaemia/infarction, Atrial fibrillation, Arrhythmia, Tachycardia, Sinus tachycardia, Palpitations	Ventricular fibrillation (rare), QT prolongation (rare), Torsade de pointes (rare), Bradycardia (rare), Vasospasm (rare)
Vascular disorders	Thrombophlebitis	Deep vein thrombosis, Hypertension, Petechiae, Hypotension, Hot flush, Peripheral coldness	
Respiratory, thoracic and mediastinal disorders	Dyspnoea, Epistaxis, Cough, Rhinorrhoea	Pulmonary embolism, Pneumothorax, Haemoptysis, Asthma, Dysphonia exertional	
Gastrointestinal disorders	Diarrhoea, Vomiting, Nausea, Stomatitis, Abdominal pain Gastrointestinal haemorrhage, Constipation, Upper abdominal pain, Dyspepsia, Abdominal pain, Dry mouth, Loose stools	Intestinal obstruction, Ascites, Enteritis, Gastritis, Dysphagia, Abdominal pain lower, Odynophagitis, Abdominal discomfort, Gastrooesophageal reflux disease, Colitis, Blood in stool	
Hepatobiliary disorders	Hyperbilirubinemia, Liver function test abnormalities	Jaundice	Hepatic failure (rare), Cholestatic hepatitis (rare)
Skin and subcutaneous tissue disorders	Palmar-plantar erythro-dysaesthesia syndrome** Rash, Alopecia, Dry skin, Pruritus, Skin hyper-pigmentation, Rash macular, Skin desquamation, Dermatitis, Pigmentation disorder, Nail disorder	Blister, Skin ulcer, Rash, Urticaria, Photosensitivity reaction, Palmar erythema, Swelling face, Purpura, Radiation recall syndrome	Cutaneous lupus erythematosus (rare), Severe skin reactions such as Stevens-Johnson syndrome and toxic Epidermal Necrolysis (very rare) (see section 4.4.)
Musculoskeletal and connective tissue disorders	Pain in extremity, Back pain, Arthralgia	Joint swelling, Bone pain, Facial pain, Musculoskeletal stiffness, Muscular weakness	
Renal and urinary disorders		Hydronephrosis, Urinary incontinence, Haematuria, Nocturia, Blood creatinine increased	
Reproductive system and breast disorders		Vaginal haemorrhage	
General disorders and administration site conditions	Fatigue, Asthenia Pyrexia, Oedema peripheral, Malaise, non cardiac chest pain	Oedema, Chills, Influenza like illness, Rigors, Body temperature increased	

** Based on the post-marketing experience, persistent or severe palmar-plantar erythrodysaesthesia syndrome can eventually lead to loss of fingerprints (see section 4.4).

Capecitabine in combination therapy:

Table 5 lists ADRs associated with the use of capecitabine in combination with different chemotherapy regimens in multiple indications based on safety data from over 3000 patients. ADRs are added to the appropriate frequency grouping (frequent or less frequent) according to the highest incidence seen in any of the major clinical trials and are not adjusted for higher frequencies that may be observed in these combination regimens. Within each system organ class grouping compared to capecitabine monotherapy (see Table 4). Uncommon ADRs reported for capecitabine in combination therapy are consistent with the ADRs reported for capecitabine monotherapy or reported for monotherapy with the combination medicinal product (in literature and/or respective summary of product characteristics).

Some of the ADRs are reactions commonly seen with the combination medicinal product (e.g. peripheral sensory neuropathy with docetaxel or oxaliplatin, hypertension seen with bevacizumab); however an exacerbation by capecitabine therapy cannot be excluded.

Table 5: Summary of related ADRs reported in patients treated with capecitabine in combination treatment in addition to those seen with capecitabine monotherapy or seen at a higher frequency grouping compared to capecitabine monotherapy

Body System	*Frequent All Grades*	*Frequency unknown (Post-Marketing Experience)*
Infections and infestations	Herpes zoster, Urinary tract infection, Oral candidiasis, Upper respiratory tract infection, Rhinitis, Influenza, Infection, Oral herpes	
Blood and lymphatic system disorders	*Neutropenia, *Leucopenia, *Anaemia, *Neutropenic fever, Thrombocytopenia Bone marrow depression, *Febrile Neutropenia	
Immune system disorders	Hypersensitivity	
Metabolism and nutrition disorders	Appetite decreased Hypokalaemia, Hyponatraemia, Hypomagnesaemia, Hypocalcaemia, Hyperglycaemia	
Psychiatric disorders	Sleep disorder, Anxiety	
Nervous system disorders	Paraesthesia, Dysaesthesia, Peripheral neuropathy, Peripheral sensory neuropathy, Dysgeusia, Headache, Taste disturbance Neurotoxicity, Tremor, Neuralgia, Hypersensitivity reaction, Hypoaesthesia	
Eye disorders	Lacrimation increased Visual disorders, Dry eye, Eye pain, Visual impairment, Vision blurred	
Ear and labyrinth disorders	Tinnitus, Hypoacusis	
Cardiac disorders	Atrial fibrillation, Cardiac ischaemia/infarction	
Vascular disorders	Lower limb oedema, Hypertension, *Embolism and thrombosis Flushing, Hypotension, Hypertensive crisis, Hot flush, Phlebitis	
Respiratory, thoracic and mediastinal system disorders	Sore throat, Dysaesthesia pharynx Hiccups, Pharyngolaryngeal pain, Dysphonia	
Gastrointestinal disorders	Constipation, Dyspepsia Upper gastrointestinal haemorrhage, Mouth ulceration, Gastritis, Abdominal distension, Gastroesophageal reflux disease, Oral pain, Dysphagia, Rectal haemorrhage, Abdominal pain lower, Oral dysaesthesia, Paraesthesia oral, Hypoaesthesia oral, Abdominal discomfort	
Hepatobiliary disorders	Hepatic function abnormal	
Skin and subcutaneous tissue disorders	Alopecia, Nail disorder Hyperhidrosis, Rash erythematous, Urticaria, Night sweats, Nail discolouration, Onycholysis	
Musculoskeletal and connective tissue disorders	Myalgia, Arthralgia, Pain in extremity Pain in jaw , Muscle spasms, Trismus, Muscular weakness	
Renal and urinary disorder	Haematuria, Proteinuria, Creatinine renal clearance decreased, Dysuria	Acute renal failure secondary to dehydration
General disorders and administration site conditions	Pyrexia, Weakness, *Lethargy, Temperature intolerance Mucosal inflammation, Pain in limb, Pain, Chills, Chest pain, Influenza-like illness, *Fever, Infusion related reaction, Injection site reaction, Infusion site pain, Injection site pain	
Injury, poisoning and procedural complications	Contusion	

* For each term, the frequency count was based on ADRs of all Grades. For terms marked with a "+", the frequency count was based on Grade 3-4 ADRs. ADRs are added according to the highest incidence seen in any of the major combination trials.

4.9 Overdosage

The manifestations of acute overdose would include nausea, vomiting, diarrhoea, gastrointestinal irritation and bleeding, and bone marrow depression. Medical management of overdose should include customary supportive medical interventions aimed at correcting the presenting clinical manifestations. Although no clinical experience using dialysis as a treatment for **AUROXEDA** overdose has been reported, dialysis may be of benefit in reducing circulating concentrations of 5-FdUrd, a low-molecular-weight metabolite of the parent compound.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A26 - Cytostatic agents

Pharmacotherapeutic group: cytostatic (antimetabolite), ATC code: L01BC06

Enzymes convert capecitabine to 5-fluorouracil (5-FU) *in vivo*. Both normal and tumor cells metabolize 5-FU to 5-fluoro-2-deoxyuridine monophosphate (FdUMP) and 5-fluorouridine triphosphate (FUTP). These metabolites cause cell injury by two different mechanisms. First, FdUMP and the folate cofactor, $N^{5,10}$-methylenetetrahydrofolate, bind to thymidylate synthase (TS). This binding results in the inhibition of TS, which is required for the synthesis of thymidine (dTMP) from uridine. Thymidine is the first building block in the thymidine triphosphate form that is essential for DNA synthesis. Without DNA, so that a deficiency of this compound can inhibit cell division. Second, nuclear transcriptional enzymes can mistakenly incorporate FUTP in place of uridine triphosphate (UTP) during the synthesis of RNA. This metabolic error can interfere with RNA processing and protein synthesis.

5.2 Pharmacokinetics properties

The pharmacokinetics of capecitabine have been evaluated over a dose range of 502 – 3 514 mg/m²/day. The parameters of capecitabine, 5'-deoxy-5-fluorouridine (5'-DFCR) and 5'-deoxy-5- fluorouridine (5'-DFUR) measured on days 1 and 14 were similar. The AUC of 5-FU was 30 % – 35 % higher on day 14. Capecitabine dose reduction decreases systemic exposure to 5-FU more than dose-proportionally, due to non-linear pharmacokinetics for the active metabolite.

Absorption:

After oral administration, capecitabine is extensively converted to the metabolites 5'- deoxy-5-fluorocytidine (5'-DFCR) and 5'-Deoxyuridine (5'-DFUR). Administration with food decreases the rate of capecitabine absorption, but only results in a minor effect on the AUC of 5'- DFUR, and on the AUC of the subsequent metabolite 5-FU. At the dose of 1 250 mg/m² on day 14 with administration after food intake, the peak plasma concentrations (C_{max}, in μg/ml) for capecitabine, 5'-DFCR, 5'-DFUR, 5-FU and FBAL were 4.67, 3.05, 12.1, 0.95 and 5,46 respectively. The time to peak plasma concentrations (T_{max} in hours) were 1.56, 2.00, 2.00, 2.00 and 3.34. The $AUC_{∞}$ values in μg.h/ml were 7. 75, 1.24, 24.6, 2.03 and 36.3.

Protein binding:

In vitro human plasma studies have determined that capecitabine, 5'-DFCR, 5'- DFUR and 5-FU are respectively 54 %, 10 %, 62 % and 10 % protein bound, mainly to albumin.

Metabolism:

Capecitabine is first metabolised by hepatic carboxylesterase to 5'-deoxy-5- fluorocytidine (5'-DFCR), which is then converted to 5'-deoxy-5-fluorouridine (5'-DFUR) by cytidine deaminase, principally located in the liver and tumour tissues. Further catalytic activation of 5'- DFUR then occurs by thymidine phosphorylase (dThdPase) to form 5-FU. Formation of 5-FU occurs preferentially at the tumor site by the tumour associated angiogenic factor dThdPase. The metabolites of capecitabine become cytotoxic after conversion to 5-FU and anabolites of 5-FU. 5-FU is further catabolised to the inactive metabolites dihydro-5-fluorouracil (FUH2), 5-fluoroureidopropionic acid (FUPA) and α-fluoro-β-alanine (FBAL) via dihydropyrimidine dehydrogenase (DPD), which is rate limiting.

Elimination:

The elimination half-life ($t_{½}$, in hours) of capecitabine, 5'-DFCR, 5'-DFUR, 5-FU and FBAL were 0,85, 1,11, 0,66, 0,76 and 3,23 respectively. The pharmacokinetics of capecitabine have been evaluated over a dose range of 502 – 3 514 mg/m²/day. The parameters of capecitabine, 5'-DFCR and 5'-DFUR measured on days 1 and 14 were similar. The AUC of 5-FU was 30 - 35 % higher on day 14, but did not increase subsequently (day 22). At therapeutic doses, the pharmacokinetics of capecitabine and its metabolites were dose proportional, except for 5-FU. After oral administration capecitabine metabolites are primarily recovered in the urine, 95,5 % of administered capecitabine dose is recovered in urine. Fecal excretion is minimal, 2,6 % of administered dose. Renal excretion of 5-FU is < 3 % of the dose. 11 % of the administered dose. About 3 % of the administered dose is excreted in urine as unchanged active ingredient, capecitabine. The interpatient variability in C_{max} and AUC of 5-FU was greater than 85 %. Combination therapy: Phase I studies evaluating the effect of **AUROXEDA** on the pharmacokinetics of either docetaxel or paclitaxel and vice versa showed no effect by **AUROXEDA** on the pharmacokinetics of docetaxel or paclitaxel (C_{max} and AUC) and no effect by docetaxel or paclitaxel on the pharmacokinetics of 5'-DFUR (the most important metabolite of capecitabine).

Pharmacokinetics in special populations:

Gender, presence or absence of liver metastasis at baseline, Karnofsky Performance Status, total bilirubin, serum albumin, ASAT and ALAT had no statistically significant effect on the pharmacokinetics of 5'-DFUR, 5-FU and FBAL in patients with colorectal cancer. Patients with hepatic impairment due to liver metastases: No clinically significant effect on the bioactivation and pharmacokinetics of capecitabine was observed in cancer patients with mildly to moderately impaired liver function due to liver metastases. There are no pharmacokinetic data in patients with severe hepatic impairment. (See section 4.2).

Patients with renal impairment:

Based on a pharmacokinetic study in cancer patients with mild to severe renal impairment, there is no evidence of an effect of creatinine clearance on the pharmacokinetics of intact active ingredient, capecitabine, and 5-FU. Creatinine clearance was found to influence the systemic exposure to 5'-DFUR (35 % increase in AUC when creatinine clearance decreases by 50 %) and to FBAL (114 % increase in AUC when creatinine clearance decreases by 50 %). FBAL is a metabolite without antiproliferative activity. 5'-DFUR is the direct precursor of 5-FU (see section 4.2., 4.3 and 4.4).

6 Pharmaceutical particulars

6.1 List of excipients

The other ingredients of **AUROXEDA** are cellulose microcrystalline, croscarmellose sodium, ferric oxide red, ferric oxide yellow, hypromellose, magnesium stearate, talc and titanium dioxide.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 months.

6.4 Special precautions for storage

Do not store above 30 °C.

Do not remove blister from carton until required for use.

6.5 Nature and contents of container

Blister pack:

PVC/PVdC with aluminium foil.

Tablets are packed in clear 250 micrometer PVC film coated with 90 g/m² PVdC as the forming material and 25 micrometer aluminium foil with 7.9 g/m² heat seal lacquer as the lidding material.

For 150 mg:

Pack size: 60s - Each carton contains 6 blisters of 10 tablets each.

For 500 mg:

Pack size: 120s - Each carton contains 12 blisters of 10 tablets each.

6.6 Special precautions for disposal and other handling

Procedures for safe handling of cytotoxic medicines should be followed.

7. Holder of certificate of registration

Aurogen South Africa (Pty) Ltd
Woodhill Office Park, Building 1, First Floor
53 Phillip Engelbrecht Avenue
Meyersdal, Ext. 12, 1448
Johannesburg
South Africa

8. Registration number

AUROXEDA 150 mg: 53/26/0100
AUROXEDA 500 mg: 53/26/0101

9. Date of first authorisation/renewal of the authorisation

Date of first authorisation: 15 December 2020

10. Date of revision of the text

21 August 2024

P1537881

✂ ⬆DETACH BEFORE DISPENSING

PASIËNTINLIGTINGSBLAD

B4

AUROXEDA 150 mg (filmbedekte tablet)
AUROXEDA 500 mg (filmbedekte tablet)

Kapesitabien

(Bevat sukker: laktosemonohidraat)

Lees hierdie hele blad noukeurig deur voordat u begin om AUROXEDA te drink.
- Hou hierdie blad. Dit mag nodig wees dat u dit weer moet lees.
- As u nog vrae het, vra asseblief vir u dokter of u apteker.
- **AUROXEDA** is vir u persoonlik voorgeskryf en u moet nie u medisyne vir ander mense gee nie. Dit kan hulle skaad, selfs al is hulle simptome dieselfde as u s'n.

Wat is hierdie blad is

1. Wat **AUROXEDA** is en waarvoor dit gebruik word
2. Wat u moet weet voordat u **AUROXEDA** drink
3. Hoe om **AUROXEDA** te drink
4. Moontlike newe-effekte
5. Hoe om **AUROXEDA** te bêre
6. Inhoud van die pak en ander inligting

1. WAT AUROXEDA IS EN WAARVOOR DIT GEBRUIK WORD

Dit bevat 'n middel genaamd kapesitabien.

Dit behoort aan 'n klas sitostatiese middels (mediisyne wat selgroei rem).

AUROXEDA word vir die behandeling van kankers, veral borskanker, kolorektale kanker en maagkanker gebruik.

2. WAT U MOET WEET VOORDAT U AUROXEDA DRINK

Moenie AUROXEDA drink nie:
- As u ook 'n allergiese reaksie op **AUROXEDA** of enige ander bestanddeel van **AUROXEDA** gehad het.
- As u 'n geskiedenis van erge onverwagte reaksies tydens behandeling met fluoorpirimidien het (dit is ook 'n middel teen kanker).
- As u ooit 'n hipersensitiwiteitsreaksie op fluorouracil (metaboliet van kapesitabien) gehad het.
- As u 'n dihidropirimidiendehidrogenaseteort het (DPD-tekort is 'n seldsame soort metaboliese afwyking).
- As u enige vorm van bloedstorms het, soos leukopenie (abnormale lae aantal witbloedselle), neutropenie (abnormale lae konsentrasie neutrofiele ('n soort witbloedsel)) of trombositopenie ('n toestand waarin u 'n lae bloedplaatjietelling het).
- As u ernstige lewersprobleme het.
- As u ernstige nierprobleme het.
- As u nou met swangerskap behandel word of in die afgelope 4 weke was of met analoë soos brivudien (dit is antivirale middels).
- As u swanger is of beplan om swanger te raak, of as u borsvoed.

Waarskuwings en voorsorgmaatreëls

Wees veral versigtig met AUROXEDA en sê vir u dokter:
- As u mediisyne wat bloed dun maak, soos warfarien, gebruik.
- As u diarree het.
- As u gedehidreer is of word as gevolg van erge naarheid en braking.
- As u hartprobleme het.
- As u lewersprobleme het.
- As u nierprobleme het.
- As u gevoelloosheid en verandertinge in sensasie, rooiheid, pyn of swelling van u hande en voete het, omdat **AUROXEDA** ook die hand-en-voetsindroom veroorsaak.

Gebruik van ander mediisyne saam met AUROXEDA

Sê altyd vir u gesondheidspraktisyn as u enige ander mediisyne gebruik (waaronder aanvullende of tradisionele mediisyne).

AUROXEDA kan 'n effek op ander mediisyne hê, of ander mediisyne kan 'n effek op **AUROXEDA** hê.
- Stolling van bloed en bloedingsparameters kan verander wanneer **AUROXEDA** saam met warfarien of fenoprokumoon gebruik word.
- Plasmakonsentrasies van fenitoïen en toksisiteitsimptome is hoër as **AUROXEDA** saam met fenitoïen (vir die behandeling van epilepsie) gebruik word.
- Die plasmakonsentrasies van **AUROXEDA** is hoër as **AUROXEDA** saam met teensuurmiddels gebruik word (teensuurmiddels is mediisyne wat die suur van die maag neutraliseer).
- Die dosis moet verlaag word as **AUROXEDA** gebruik word saam met folensuur (verminder die toksiese effekte van metotreksaat en pirimetamien) of interferon alfa (mediisyne wat gebruik word vir die behandeling van virale infeksies en kankers).
- As u tans met radioterapie behandel word of 'n geskiedenis daarvan het, is dit meer waarskynlik dat u newe-effekte sal ervaar.
- 'n Moontlike lewensbedreigende interaksie kan ontstaan as **AUROXEDA** en sirovudien of die chemiese verwante analoë daarvan soos brivudien, saam gebruik word en daarom moet dit nie gedoen word nie.

Gebruik van AUROXEDA saam met voedsel en drank

AUROXEDA moet 30 minute na 'n ete met water gedrink word.

Swangerskap en borsvoeding

As u swanger is of u baba borsvoed, moet u asseblief vir u dokter, apteker of ander gesondheidspraktisyn om advies vra voordat u **AUROXEDA** drink.

AUROXEDA word nie tydens swangerskap of borsvoeding aanbeveel nie, aangesien **AUROXEDA** skadelik vir die baba kan wees (kyk "Moenie **AUROXEDA** drink nie").

Sowel mans as vrouens moet seker maak dat voldoende geboortebeperkingsmaatreëls toegepas word terwyl hulle **AUROXEDA** ontvang. Jou dokter gaan jou raadgee oor die metode van voorbehandeling om te gebruik en hoe lank dit gebruik moet word. Voorbehoeding word tipies vir 3 maande na voltooiing van **AUROXEDA**-behandeling by mans en vir 6 12 maande na voltooiing van **AUROXEDA**-behandeling by vrouens toegepas.

Motorbestuur en gebruik van masjinerie

Aangesien **AUROXEDA** duiseligheid ('n gevoel dat jy wil omval), moegheid en visieprobleme kan veroorsaak, kan dit u vermoë om te 'n voertuig te bestuur, masjinerie te gebruik of enige ander take te doen wat konsentrasie benodig, beïnvloed.

AUROXEDA bevat laktose

AUROXEDA bevat laktose wat 'n tipe suiker is. As u dokter dus vir u gesê het dat u 'n onverdraagbaarheid teenoor sekere suikers het, moet u u dokter skakel voordat u hierdie mediisyne drink.

3. HOE OM AUROXEDA TE DRINK

Moenie mediisyne wat vir u voorgeskryf is vir enige ander persoon gee nie.

Drink **AUROXEDA** altyd presies soos wat u dokter vir u gesê het. Raadpleeg u dokter of apteker as u nie seker is nie.

Die aanbevole dosis kan afhang van die tipe en erns van u kanker, u ouderdom en u liggaamsoppervlakte.

AUROXEDA moet 30 minute na 'n ete met 'n glas water afgesluk word.

U dokter sal vir u sê hoe lank u behandeling met **AUROXEDA** sal duur. Moenie die behandeling vroeg stop nie, want dit kan maak dat u toestand weer terugkeer. Sê vir u dokter of apteker as u die indruk het dat die effek van **AUROXEDA** te sterk of te swak is.

As u meer AUROXEDA gedrink het as wat u moes

As u meer as die nodige dosis drink, kan u naarheid, braking, diarree (gereeld en waterige stoelgange), mukositis (slymvliesontsteking), gastro-intestinale irritasie, bloeding en beenmurgonderdrukking ervaar.

Simptomatiese en ondersteunende maatreëls moet verskaf word.

Raadpleeg u dokter of apteker in geval van oordosering. As nie een beskikbaar is nie, kontak die naaste hospitaal of *gifsentrum*.

As u vergeet om AUROXEDA te drink

As u vergeet om 'n dosis te drink, drink dit sodra as wat u dit onthou, behalwe as dit bykans tyd vir u volgende dosis is. Moenie 'n dubbele dosis drink om vir vergete individuele dosisse op te maak nie.

4. MOONTLIKE NEWE-EFFEKTE

Nie al die newe-effekte wat vir **AUROXEDA** aangemeld is, is in hierdie blad opgeneem nie. As u algemene gesondheidstoestand vererger of as u newe-effekte ervaar terwyl u hierdie mediisyne gebruik, moet u u dokter, apteker of ander gesondheidsdiensverskaffer om advies raadpleeg.

AUROXEDA kan newe-effekte veroorsaak.

Indien enige van die volgende voorkom, moet u ophou om **AUROXEDA** te drink en onmiddellik vir u dokter sê of na die naaste noodafdeling van u naaste hospitaal gaan:
- swelling van die hande, voete, enkels, gesig, lippe, mond of keel wat probleme met sluk kan veroorsaak
- pruritus ('n intense jeukensasie)
- verkleuring van die vel
- uitwerpsel van die vel of blase op die vel, mond, oë of geslagsdele, aangesien dit kan wees vanweë 'n ernstige allergiese reaksie bekend as Stevens-Johnsonsindroom.

Dit is almal baie ernstige newe-effekte. As u dit ervaar, kan dit wees dat u 'n ernstige allergiese reaksie op **AUROXEDA** het. Dit mag wees dat u dringende mediese aandag of hospitaalsorge nodig het.

Sê vir u dokter as u enige van die volgende opmerk:

Newe-effekte wat dikwels voorkom:
- daling in die aantal rooibloedselle, witbloedselle en bloedplaatjies (in bloedtoetse gesien)
- vereis aan eetlus
- bulk- of maagpyn
- liggaam of enige diarree (tos of waterige stoelgang)
- stomatitis (sere in die mond en keel)
- hardnyheid (moeilike ontlasting van die ingewande), lig of matig
- naarheid
- ongewone moegheid
- braking
- hiperbilirubinemie [groot hoeveelhede galpigment (bilirubien) in die bloed]
- dermatitis (ontsteking van die vel)
- hand-voet-sindroom (rooiheid, swelling en pyn in die handpalms en/of voetsole)

Newe-effekte wat minder dikwels voorkom:
- enkefalopatie (breinverwante siekte of afwyking)
- swaminfeksies
- infeksie
- keratokonjunktivitis (ontsteking van die kornea en konjunktiva)
- sepsis (ernstervormende bakteriële of fout gifbesware in die bloed of weefsel)
- virusinfeksie.
- griepagtige siekte
- geïrriteerdheid
- stollingsversteuring (bloedstollingsversteuring)
- leukopenie (abnormale lae witbloedselletelling)
- limfedeem (linf wat in die weefsel ophoop)
- hipokalsiëmie (lae kalsium in die bloed)
- hipomagnesemie (laer magnesiumkonsentrasie in serum)
- hiperglukemie (hoë bloedglukosevlakke (suikervlakke in die bloed)
- dehidrasie (uitputting van liggaamsvloeistowwe)
- vertes van bewussyn
- duiseligheid ('n gevoel dat jy wil omval)
- insomnia (chroniese slaaploosheid)
- verwardheid
- depressie
- ataksie (swermoot om vrywillige spierbewegings te koördineer)
- hoofpyn
- parestesie (abnormale velsensasies)
- swak balans
- bewing (onwillekeurige vibrasie)
- vereltis (ontsteking van die konjunktiva van die oë)
- irritasie van die oë
- angina pectoris (bloedstand gekenmerk deur pyn op die bors)
- atriale fibrillasie
- bradikardie (abnormaal stadige hartklop)
- kardiomiopatie (hartspierversteuring)
- kardiotoksisiteit (beskadiging van die hartspier)
- ekstrasistole (hartklop buite die normale ritme)
- miokarditis (ontsteking van die miokardium van die hart)
- perikardiale effusie (vloeistof rondom die hart)
- taglikardie (abnormaal vinnige hartklop)
- ventrikulêre ekstrasistole (ekstra abnormale hartklop wat in een ventrikel begin)
- serebrovaskulêre ongeluk
- hipotensie (abnormale lae bloeddruk)
- hipertensie (abnormale hoë bloeddruk)
- flebitis (ontsteking van 'n aar gewoonlik in die bene)
- tromboflebitis (saam met die vorming van 'n bloedklont)
- diepaarttrombose
- warm gloede (skielike kort gevoel van hitte)
- bronngitis (ontsteking van bronguis)
- bronngospasme (vernouing van die wande van die longe)
- bronngospasma (spasma van die bronqi wat uitasemning moeilik en raserig maak)
- dispnee (moeilike of swaar asemhaling)
- respiratoriese ongemak
- disartrie (swak spraakvermoë)
- epistaksie (bloeding uit die neusgat neuhoite of nasofarinks)
- hemoptise (hoes van bloed of bloedbevlekte slym vanuit die bronqi larinks tragea of longe)
- longontsteking (ontsteking van die longweefsels)
- longembolie (verstopping van die longslagaar)
- asma (ontsteking en vernouing van die lugweë)
- hoes
- heesheid (hardheid in die keel)
- laringitis (ontsteking van die larinks)
- disfasie (taalstoornis wat gekenmerk word deur 'n gebrek in die generering van spraak)
- maagseer
- gastro-intestinale bloeding (bloeding in die spysverteringskanaal)
- toksisiteit in die gastro-intestinale weg
- hemorragie (bloeding)
- ileus (verstopping van die ingewande - veral die ileum)
- disperpsie (versteuring van spysverteringsfunksie)
- buikdistensie (lug (gas) of vloeistof hoop op in die buik)
- abnormale kodonfrekwensie
- assites (opeenhoping van sereuse vloeistof in die buikholte)
- gastro-enteritis (ontsteking van die maag en ingewande)
- versteurings in gastro-intestinale beweging
- cholestatiese hepatitis (verstopping van die galbuise buite die lewer)
- lewerfibrose of hepatitis (ontsteking van die lewer)
- fotosensitiwiteit (sensitiwiteit vir lig)
- hernoep van stralingseffekte (ernstige velreaksie wat voorkom wanneer sekere chemoterapie-middels tydens of kort na behandeling met bestraling toegedien word)
- versteurings van die naels
- meer sweet
- beenmurgonderdrukking
- artralgie (pyn in 'n gewrig)
- rugpyn
- artritis (ontsteking van een of meer gewrigte)
- pyn in die skeletbene
- probleme om te loop
- fibrose (ontwikkeling van oortollige veselagtige bindweefsel in 'n orgaan)
- spierswakheid
- swak nierfunksie (nierprobleme)
- proktalgie (toestand waarin die riere die vermoë verloor om afval te verwyder en vloeistowwe te balanseer)
- inenstorting
- koors
- koors (hoë liggaamstemperatuur - koors)
- ckrs ('n gevoel nood of behoefte om iets te drink)
- toename in gewig.

As u enige newe-effekte opmerk wat nie in hierdie blad genoem word nie, moet u u dokter of apteker asseblief in kennis stel.

Aanmeld van newe-effekte

Praat met u dokter, apteker of verpleegkundige as u enige newe-effekte kry. Dit sluit alle moontlike newe-effekte in wat nie in hierdie blad gelys word nie. U kan newe-effekte ook by SAHPRA aanmeld via die vorm '6.04 Adverse Drug Reaction Reporting Form" wat aanlyn onder SAHPRA se publikasies gekry kan word: https://www.sahpra.org.za/Publications/Index/8. Deur newe-effekte aan te meld, kan u help om meer inligting oor die veiligheid van **AUROXEDA** te gee.

5. HOE OM AUROXEDA TE BÊRE

Bêre by of onder 30 °C.

Hou die stulpstroke in die karton totdat dit benodig word.

HOU ALLE MEDISYNE BUITE BEREIK VAN KINDERS.

Gee alle ongebruikte mediisyne terug aan u apteker.
Ongebruikte mediisyne moet nie in dreinering- of rioolsisteels (bv. toilette) gegooi word nie.

6. INHOUD VAN DIE PAK EN ANDER INLIGTING

Wat AUROXEDA bevat

Die aktiewe bestanddeel is kapesitabien.

AUROXEDA 150 mg:

Elke filmbedekte tablet bevat 150 mg kapesitabien. Bevat suiker: 19,99 mg sukrose

AUROXEDA 500 mg:

Elke filmbedekte tablet bevat 500 mg kapesitabien. Bevat suiker: 66,65 mg sukrose.

Die ander bestanddele van **AUROXEDA** is mikrokristalline sellulose, natriumkruskarmellose, rooi ysteroksiede, geel ysteroksiede, hipromellose, watervrye laktose, magnesiumstearaat, talk en titaandioksiede.

Hoe AUROXEDA lyk en die inhoud van die pakkie

AUROXEDA 150 mg:

Ligte persikokleurige, bikonvekse, langwerpige filmbedekte tablette met 150 op een kant gedruk en die ander kant skoon.

AUROXEDA 500 mg:

Persikokleurige, bikonvekse, langwerpige filmbedekte tablette met 500 op een kant gedruk en die ander kant skoon.

Stulppak:

Tablette word verpak in 'n helder PVC-film van 250 mikrometer wat bedek is met 90 g/m² PVdC as die vormende materiaal en aluminiumfoelie van 25 mikrometer met 7 g/m² hitte-seëllak as dekmateriaal.

Vir 150 mg:

Pakgrootte: 60 tablette - elke karton bevat 6 stulpstroke met 10 tablette elk.

Vir 500 mg:

Pakgrootte: 120 tablette - elke karton bevat 12 stulpstroke met 10 tablette elk.

Registrasiehouer

Aurogen South Africa (Edms) Bpk
Woodhillkantoorpark, Gebou 1, Eerste vloer
53 Phillip Engelbrechtlaan 53
Meyersdal Uitbr. 12, 1448
Johannesburg
Suid-Afrika

Hierdie blad is hersien op

21 Augustus 2024

Registrasienommers

AUROXEDA 150 mg: 53/26/0100
AUROXEDA 500 mg: 53/26/0101

P1537881