

**Approved Professional Information for Medicines for Human Use:
AUSTELL CITALOPRAM**

SCHEDULING STATUS

S5

1. NAME OF THE MEDICINE

AUSTELL CITALOPRAM 10 mg film-coated tablets

AUSTELL CITALOPRAM 20 mg film-coated tablets

AUSTELL CITALOPRAM 40 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

AUSTELL CITALOPRAM 10 mg

Each film-coated tablet contains citalopram hydrobromide 12,495 mg equivalent to citalopram 10 mg.

Contains sugar (lactose monohydrate): 23,64 mg per tablet.

AUSTELL CITALOPRAM 20 mg

Each film-coated tablet contains citalopram hydrobromide 24,990 mg equivalent to citalopram 20 mg.

Contains sugar (lactose monohydrate): 47,27 mg per tablet.

AUSTELL CITALOPRAM 40 mg

Each film-coated tablet contains citalopram hydrobromide 49,980 mg equivalent to citalopram 40 mg.

Contains sugar (lactose monohydrate): 94,54 mg per tablet.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

AUSTELL CITALOPRAM 10 mg FILM-COATED TABLETS

White to off-white, round, plain, film-coated tablets.

AUSTELL CITALOPRAM 20 mg FILM-COATED TABLETS

White to off-white, oval, biconvex, film-coated tablets with 'BL' embossed on one side, and '20' on the other.

AUSTELL CITALOPRAM 40 mg FILM-COATED TABLETS

White to off-white, oval, biconvex, film-coated tablets with 'BL' embossed on one side and '40' on the other.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AUSTELL CITALOPRAM is indicated for the treatment of:

- Depression and prevention of relapse.
- Panic disorders with or without agoraphobia.
- Obsessive-compulsive disorder (OCD).

4.2 Posology and method of administration

Posology

Treating Depression

20 mg a day as a single dose. Dosage may be increased by 20 mg a day at intervals of at least one week to a maximum of 40 mg depending on the patient's response.

Duration of treatment

The antidepressant effect usually sets in after 2 to 4 weeks.

Treatment with AUSTELL CITALOPRAM is symptomatic and must therefore be continued for an appropriate length of times, usually up to 6 months after recovery in order to prevent relapse.

Treating Panic Disorder

10 mg a day as a single dose for the first week then increased to 20 mg a day. The dose may be increased thereafter as required to a maximum of 40 mg a day depending on the patient's response.

Treating Obsessive Compulsive Disorder (OCD)

20 mg a day as a single dose. This dose can be increased by 20 mg increments to a maximum of 40 mg a day depending on the patient's response.

Duration of treatment

The onset of action in treating OCD is 2 – 4 weeks with further improvement over time.

Special populations

Elderly patients (> 65 years of age)

For elderly patients the dose should be decreased to half of the recommended dose, e.g., 10 – 20 mg daily. The recommended maximum dose for the elderly is 20 mg daily.

Renal impairment

Dose adjustment is not necessary in cases of mild or moderate renal impairment.

AUSTELL CITALOPRAM is contraindicated in patients with severe renal impairment (creatinine clearance less than 30 mL/min) (see section 4.3 and 5.2)

Hepatic impairment

An initial dose of 10 mg daily for the first two weeks of treatment is recommended in patients with mild or moderate hepatic impairment. Depending on individual patient response, the dose may be increased to a maximum of 20 mg daily. Caution and extra careful dose titration is advised in patients with severely reduced hepatic function.

Poor metabolisers of CYP2C19

An initial dose of 10 mg daily during the first two weeks of treatment is recommended for patients who are known to be poor metabolisers with respect to CYP2C19. The dose may be increased to a maximum of 20 mg daily depending on individual patient response.

Withdrawal symptoms seen on discontinuation

Abrupt discontinuation should be avoided. When stopping treatment with AUSTELL CITALOPRAM the dose should be gradually reduced over a period of at least one or two weeks in order to reduce the risk of withdrawal symptoms (see section 4.4 and 4.8).

If intolerable symptoms occur following a decrease in the dose or upon discontinuation of treatment, then resuming the previously prescribed dose may be considered. Subsequently, the medical practitioner may continue decreasing the dose, but at a more gradual rate.

Paediatric population

AUSTELL CITALOPRAM should not be used in the treatment of children and adolescents under the age of 18 years (see section 4.3 and 4.4)

Method of administration

AUSTELL CITALOPRAM tablets are administered as a single daily (oral) dose.

AUSTELL CITALOPRAM should be gradually withdrawn during a couple of weeks when stopping therapy (see section 4.4).

AUSTELL CITALOPRAM may be taken with or without food in the morning or evening.

4.3 Contraindications

- Hypersensitivity to citalopram or any of the excipients listed in section 6.1.
- AUSTELL CITALOPRAM is contraindicated in children and adolescents under the age of 18 years (see section 4.4)

- MAOIs (monoamine oxidase inhibitor):
Cases of serious and sometimes fatal reactions have been reported in patients receiving and SSRI in combination with a MAOI, including selective MAO-B inhibitor selegiline and the reversible MAOI (RIMA) moclobemide and in patients who have discontinued an SSRI and have been started on a MAOI.
Some cases presented with features resembling serotonin syndrome.
- AUSTELL CITALOPRAM must not be used in combination with a MOAI, including selegiline in doses above 10 mg daily.
- At least 14 days should elapse between discontinuing the non-selective MAOI and minimum one day after discontinuation of moclobemide before initiating therapy with AUSTELL CITALOPRAM. MAOIs should not be introduced for 7 days after discontinuation of AUSTELL CITALOPRAM (see section 4.5).
- AUSTELL CITALOPRAM is contraindicated in combination with linezolid.
- AUSTELL CITALOPRAM should not be used concomitantly with pimozide (see section 4.5).
- Severe renal impairment (creatinine clearance less than 30 mL/min).
- AUSTELL CITALOPRAM is contraindicated in patients with known QT-interval prolongation or congenital long QT syndrome.
- AUSTELL CITALOPRAM is contraindicated together with medicines that are known to prolong the QT-interval (see section 4.5).
- Safety and efficacy in pregnancy and lactation has not been established (see section 4.6).

4.4 Special warnings and precautions for use

Suicidality

Patients with major depressive disorder, both adults and children, may experience worsening of their depression and or the emergence of suicidal ideation and behaviour, whether or not they are taking antidepressant medicines. This risk may persist until significant remission occurs. Patients should be

monitored during early therapy until improvement in depression is observed because suicide is an inherent risk in depressed patients.

A causal role, however, for antidepressant medicines in inducing such behaviour has not been established. Patients being treated with AUSTELL CITALOPRAM should, nevertheless, be observed closely for clinical worsening and suicidality, especially at the beginning of a course of therapy, or at any time of dose changes, either increases or decreases. Because of the possibility of co-morbidity between major depressive disorder and other psychiatric and non-psychiatric disorders, the same precautions observed when treating patients with major depressive disorder should be observed when treating patients with other psychiatric and non-psychiatric disorders.

The following symptoms have been reported in patients being treated with antidepressants for major depressive disorder as well as for other indications, both psychiatric and non-psychiatric: anxiety, agitation, panic attacks, insomnia, irritability, hostility (aggressiveness, impulsivity, akathisia, hypomania and mania). Although a causal link between the emergence of such symptoms and either the worsening of depression and/or the emergence of suicidal impulses has not been established, consideration should be given to changing the therapeutic regimen, including possibly discontinuing AUSTELL CITALOPRAM, in patients for whom such symptoms are severe, abrupt in onset, or were not part of the patient's presenting symptoms.

Withdrawal symptoms seen on discontinuation of SSRI treatment

If the decision is made to discontinue treatment, AUSTELL CITALOPRAM should be tapered (see section 4.2).

Withdrawal symptoms when treatment is discontinued are common, particularly if discontinuation is abrupt (see section 4.8).

The risk of withdrawal symptoms may be dependent on several factors including the duration and dose of therapy and the rate of dose reduction. Dizziness, sensory disturbances (including paraesthesia), sleep

disturbances (including insomnia and intense dreams), agitation or anxiety, nausea and/or vomiting, tremor, confusion, sweating, headache, diarrhoea, palpitations, emotional instability, irritability, and visual disturbances are the most commonly reported reactions. Generally, these symptoms are mild to moderate, however, in some patients they may be severe in intensity. They usually occur within the first few days of discontinuing treatment, but there have been very rare reports of such symptoms in patients who have inadvertently missed a dose. Generally, these symptoms are self-limiting and usually resolve within 2 weeks, though in some individuals they may be prolonged (2-3 months or more). It is therefore advised that citalopram should be gradually tapered when discontinuing treatment over a period of several weeks or months, according to the patient's needs (see "Withdrawal symptoms seen on discontinuation of citalopram", section 4.2)

AUSTELL CITALOPRAM should be used with caution in:

Elderly patients

- Elderly patients because of a longer half-life and decreased clearance due to a reduced rate of metabolism.

A lower dose is recommended in the elderly (see section 4.2).

Reduced liver function

- Hepatic impairment - Clearance of AUSTELL CITALOPRAM is reduced. Cautious dosage titration and a lower maximum dose are recommended.

Reduced kidney function

- Renal impairment - Elimination is decreased. If creatine clearance is less than 30 mL/min AUSTELL CITALOPRAM should not be used (see section 4.3).

Seizures or history thereof

- There is an increased risk of seizures. AUSTELL CITALOPRAM should be used with caution in patients with controlled epilepsy and avoided in patients who are poorly controlled epileptics. Care is advised in patients receiving electroconvulsive therapy.

Mania or history of mania

- In patients with manic-depressive illness a change towards the manic phase may occur. Condition may be re-activated. AUSTELL CITALOPRAM should be discontinued if the patient enters the manic phase.

Paradoxical anxiety

- Some patients with panic disorder may experience intensified anxiety symptoms at the start of treatment with antidepressants. This paradoxical reaction usually subsides within the first two weeks of starting treatment. A low starting dose is advised to reduce the likelihood of a paradoxical anxiogenic effect (see section 4.2).

Psychosis

- Treatment of psychotic patients with depressive episodes may increase psychotic symptoms.

Bradycardia

- AUSTELL CITALOPRAM may cause a reduction in heart rate. Caution is advised in patients with a pre-existing slow heartrate.

Diabetes mellitus

- Occurrences of hypoglycaemia have been reported. In patients with diabetes, treatment with an SSRI may alter glycaemic control. Insulin and/or oral hypoglycaemic dosage may need to be adjusted.

Other medicines

- AUSTELL CITALOPRAM should not be used with monoamine oxidase inhibitors; imipramine; moclobemide; alcohol; warfarin; and cimetidine (see section 4.3 and 4.5).
- Citalopram should not be used concomitantly with medicines with serotonergic effects such as sumatriptan or other triptans, tramadol, oxitriptan and tryptophan (see section 4.3 and 4.5).
- Undesirable effects may be more common during concomitant use of citalopram and herbal preparations containing St John's wort (*Hypericum perforatum*). Therefore, citalopram and St John's wort preparations should not be taken concomitantly (see section 4.3 and 4.5).

Haemorrhage

- There have been reports of prolonged bleeding time and /or bleeding abnormalities such as ecchymoses, gynaecological haemorrhages, gastrointestinal bleeding and other cutaneous or mucous bleedings with SSRIs (see section 4.8).
- SSRIs/SNRIs may increase the risk of postpartum haemorrhage (see sections 4.6 and 4.8).
- Caution is advised in patients taking SSRIs, particularly with concomitant use of active ingredients known to affect platelet function or other active ingredients that can increase the risk of haemorrhage, as well as in patients with a history of bleeding disorders (see section 4.5).

QT-interval prolongation

- AUSTELL CITALOPRAM may cause a dose-dependent prolongation of the QT-interval. Cases of QT interval prolongation and ventricular dysrhythmia including torsade de pointes have been reported during the post-marketing period, predominantly in patients of female gender, with hypokalaemia, or with pre-existing QT prolongation or other cardiac diseases (see section 4.3, 4.5, 4.8 and 4.9).
- Caution is advised in patients with significant bradycardia; or in patients with recent acute myocardial infarction or uncompensated heart failure.
- Electrolyte disturbances such as hypokalaemia and hypomagnesaemia increase the risk for malignant dysrhythmias and should be corrected before treatment with AUSTELL CITALOPRAM is started.

- If patients with stable cardiac disease are treated, an ECG review should be considered before treatment is started.
- ECG monitoring may be advisable in case of overdose or conditions of altered metabolism with increased peak levels, e.g. liver impairment.
- If signs of cardiac dysrhythmia occur during treatment with AUSTELL CITALOPRAM, the treatment should be withdrawn, and an ECG should be performed.

Serotonin syndrome

- Serotonin syndrome is more likely to occur after an increase in dose.
- A combination of symptoms such as agitation, tremor, myoclonus and hyperthermia may indicate the development of this condition (see section 4.5).
- Treatment with citalopram should be discontinued immediately and symptomatic treatment initiated.

Hyponatraemia

- Hyponatraemia, probably due to inappropriate antidiuretic hormone secretion (SIADH), has been reported with the use of SSRIs and generally reverses on discontinuation of therapy. Elderly female patients seem to be at particularly high risk.

Akathisia/psychomotor restlessness

- The use of SSRIs/SNRIs has been associated with the development of akathisia, characterised by a subjectively unpleasant or distressing restlessness and need to move often accompanied by an inability to sit or stand still. This is most likely to occur within the first few weeks of treatment. In patients who develop these symptoms, increasing the dose may be detrimental.

Angle-closure Glaucoma

- SSRIs including citalopram may have an effect on pupil size resulting in mydriasis. This mydriatic effect has the potential to narrow the eye angle resulting in increased intraocular pressure and angle-

closure glaucoma, especially in patients pre-disposed. Citalopram should therefore be used with caution in patients with angle-closure glaucoma or history of glaucoma.

Sexual dysfunction

Selective serotonin reuptake inhibitors (SSRIs/serotonin norepinephrine reuptake inhibitors (SNRIs) may cause symptoms of sexual dysfunction (see section 4.8). There have been reports of long-lasting sexual dysfunction where the symptoms have continued despite discontinuation of SSRIs/SNRI.

Paediatric population

AUSTELL CITALOPRAM should not be used in the treatment of children and adolescents under the age of 18 years. In clinical trials in Major Depressive Disorder, there were increased reports of hostility (predominantly aggression, oppositional behaviour, and anger) and suicide-related adverse events such as suicidal ideation and self-harm (see section 4.3).

In addition, long-term safety data in children and adolescents concerning growth, maturation and cognitive and behavioural development are lacking.

Excipients: galactose intolerance

AUSTELL CITALOPRAM contains lactose monohydrate: patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take AUSTELL CITALOPRAM.

4.5 Interaction with other medicines and other forms of interaction

Pharmacodynamic interactions

At the pharmacodynamic level cases of serotonin syndrome with citalopram and moclobemide and buspirone have been reported.

Contraindicated combinations

Monoamine oxidase inhibitors (MAOI)

Concurrent use is contra-indicated. Serious and potentially fatal reactions have occurred such as: hyperthermia, rigidity, myoclonus, autonomic instability with rapid fluctuation of vital signs and mental status changes including extreme agitation progressing to delirium and coma (see section 4.3).

QT interval prolongation

Pharmacokinetic and pharmacodynamic studies between citalopram and other medicines that prolong the QT interval have not been performed. An additive effect of citalopram and these medicines cannot be excluded. Therefore, co-administration of citalopram with medicines that prolong the QT interval, such as Class IA and III antidysrhythmics, antipsychotics (e.g. phenothiazine derivatives, pimozide, haloperidol), tricyclic antidepressants, certain antimicrobial medicines (e.g. sparfloxacin, moxifloxacin, erythromycin IV, pentamidine, anti-malarial treatment particularly halofantrine), certain antihistamines (astemizole, mizolastine) etc., is contraindicated.

Pimozide

Co-administration of a single dose of pimozide 2 mg to subjects treated with racemic citalopram 40 mg/day for 11 days caused an increase in AUC and C_{max} of pimozide, although not consistently throughout the study. The co-administration of pimozide and citalopram resulted in a mean increase in the QTc interval of approximately 10 msec. Due to the interaction noted at a low dose of pimozide, concomitant administration of citalopram and pimozide is contraindicated.

Combinations requiring precautions for use

Selegiline (selective MAO-B inhibitor)

A reported pharmacokinetic / pharmacodynamic interaction study with concomitantly administered citalopram (20 mg daily) and selegiline (10 mg daily) (a selective MAO B inhibitor) demonstrated no clinically relevant interactions. The concomitant use of citalopram and selegiline (in doses above 10 mg daily) is not recommended (see section 4.3)

Serotonergic medicines or medicines with serotonergic activity

Lithium and tryptophan

No pharmacodynamic interactions have been found in reported clinical studies in which citalopram has been given concomitantly with lithium. However there have been reports of enhanced effects when SSRIs have been given with lithium or tryptophan and therefore concomitant use of citalopram with these medicines predicts should be undertaken with caution. Routine monitoring of lithium levels should be continued as usual.

Co-administration with serotonergic medicines (e.g. tramadol, sumatriptan) may lead to enhancement of 5-HT associated effects. Increased risk of developing the serotonin syndrome, a rare but potentially fatal hyperserotonergic state.

The simultaneous use of AUSTELL CITALOPRAM and 5-HT agonists, such as sumatriptan and other triptans, is not recommended (see section 4.4).

St. John's wort

Dynamic interactions between SSRIs and the herbal remedy St John's wort (*Hypericum perforatum*) can occur, resulting in an increase in undesirable effects (see section 4.4). Pharmacokinetic interactions have not been investigated.

Haemorrhage

Caution is warranted for patients who are being treated simultaneously with anticoagulants, medicines that affect the platelet function, such as non-steroidal anti-inflammatory drugs (NSAIDs), acetylsalicylic acid, dipyridamole, and ticlopidine or other medicines (e.g. atypical antipsychotics) that can increase the risk of haemorrhage (see section 4.4). *Warfarin* – the anticoagulant activity of warfarin may be increased.

ECT (electroconvulsive therapy)

There are no clinical studies establishing the risks or benefits of the combined use of electroconvulsive therapy (ECT) and citalopram (see section 4.4).

Alcohol

No pharmacodynamic or pharmacokinetic interactions have been demonstrated between citalopram and alcohol. However, the combination of citalopram and alcohol is not advisable. The effects of alcohol may be increased.

Medicines inducing hypokalaemia/hypomagnesaemia

Caution is warranted for concomitant use of hypokalaemia- / hypomagnesaemia-inducing medicines as these conditions increase the risk of malignant dysrhythmias.

Medicines lowering the seizure threshold

SSRIs can lower the seizure threshold. Caution is advised when concomitantly using other medicines capable of lowering the seizure threshold (e.g. antidepressants [SSRIs], neuroleptics [thioxanthenes and butyrophenones]), mefloquine, bupropion and tramadol).

Pharmacokinetic interactions

Biotransformation of citalopram to demethylcitalopram is mediated by CYP2C19 (approx. 38 %), CYP3A4 (approx. 31 %) and CYP2D6 (approx. 31 %) isozymes of the cytochrome P450 system. The fact that citalopram is metabolised by more than one CYP means that inhibition of its biotransformation is less likely as inhibition of one enzyme may be compensated by another. Therefore, co-administration of citalopram with other medicines in clinical practice has very low likelihood of producing pharmacokinetic medicine interactions.

Food

The absorption and other pharmacokinetic properties of citalopram have not been reported to be affected by food.

Effect of other medicines on the pharmacokinetics of citalopram

Co-administration with ketoconazole (potent CYP3A4 inhibitor) did not change the pharmacokinetics of citalopram.

A reported pharmacokinetic interaction study of lithium and citalopram did not reveal any pharmacokinetic interactions (see also above).

Cimetidine

Cimetidine (potent CYP2D6, 3A4 and 1A2 inhibitor) caused a moderate increase in the average steady state levels of citalopram. Caution is advised when administering citalopram in combination with cimetidine. Dose adjustment may be warranted.

Co-administration of escitalopram (the active enantiomer of citalopram) with omeprazole 30 mg once daily (a CYP2C19 inhibitor) resulted in moderate (approximately 50 %) increase in the plasma concentrations of escitalopram.

Thus, caution should be exercised when used concomitantly with CYP2C19 inhibitors (e.g., omeprazole, esomeprazole, fluconazole, fluvoxamine, lansoprazole, ticlopidine) or cimetidine. A reduction in the dose of citalopram may be necessary based on monitoring of side-effects during concomitant treatment (see section 4.4).

Metoprolol

Escitalopram (the active enantiomer of citalopram) is an inhibitor of the enzyme CYP2D6. Caution is recommended when citalopram is co-administered with medicines that are mainly metabolised by this enzyme, and that have a narrow therapeutic index, e.g. flecainide, propafenone and metoprolol (when used in cardiac failure), or some CNS acting medicines that are mainly metabolised by CYP2D6, e.g. antidepressants such as desipramine, clomipramine and nortriptyline or antipsychotics like risperidone,

thioridazine and haloperidol. Dosage adjustment maybe warranted. Co-administration with metoprolol resulted in a twofold increase in the plasma levels of metoprolol but did not statistically significant increase the effect of metoprolol on the blood pressure and cardiac rhythm.

Effects of citalopram on other medicines

A reported pharmacokinetic / pharmacodynamic interaction study with concomitant administration of citalopram and metoprolol (a CYP2D6 substrate) showed a twofold increase in metoprolol concentrations, but no statistically significant increase in the effect of metoprolol on blood pressure and heart rate in healthy volunteers.

Citalopram and demethylcitalopram are negligible inhibitors of CYP2C9, CYP2E1 and CYP3A4, and only weak inhibitors of CYP1A2, CYP2C19 and CYP2D6 as compared to other SSRIs established as significant inhibitors.

Levomepromazine, digoxin, carbamazepine

No change or only very small changes of clinical importance were observed when citalopram was given with CYP1A2 substrates (clozapine and theophylline), CYP2C9 (warfarin), CYP2C19 (imipramine and mephenytoin), CYP2D6 (sparteine, imipramine, amitriptyline, risperidone) and CYP3A4 (warfarin, carbamazepine (and its metabolite carbamazepine epoxid) and triazolam).

No pharmacokinetic interaction was observed between citalopram and levomepromazine, or digoxin, (indicating that citalopram neither induces nor inhibits P-glycoprotein).

Desipramine, imipramine

In a reported pharmacokinetic study, no effect was demonstrated on either citalopram or imipramine levels, although the level of desipramine, the primary metabolite of imipramine was increased. When desipramine is combined with citalopram, an increase of the desipramine plasma concentration has been observed. A reduction of the desipramine dose may be needed.

Tricyclic antidepressants

It appears that AUSTELL CITALOPRAM does not cause a marked increase in plasma levels of some tricyclic antidepressants.

4.6 Fertility, pregnancy and lactation

Pregnancy

Safety and efficacy in pregnancy and lactation has not been established.

Citalopram should not be used during pregnancy unless clearly required and only following careful consideration of risk/benefit. Abrupt discontinuation of citalopram should be avoided during pregnancy.

Should maternal use of citalopram continue into the later stages of pregnancy, particularly into the third trimester, neonates should be observed following birth.

The following symptoms may occur in the neonates following maternal use of SSRI/SNRI use in later stages of pregnancy: respiratory distress, cyanosis, apnoea, seizures, temperature instability, feeding difficulty, vomiting, hypoglycaemia, hypertonia, hypotonia, hyperreflexia, tremor, jitteriness, irritability, lethargy, constant crying, somnolence and difficulty sleeping. These symptoms could be due to either serotonergic effects or discontinuation symptoms and in the majority of instances complications begin immediately or shortly (< 24 hours) following delivery.

Use of SSRIs in pregnancy, particularly in late pregnancy, may increase the risk of persistent pulmonary hypertension in the newborn (PPHN).

Observational data indicate an increased risk (less than 2-fold) of postpartum haemorrhage following SSRI/SNRI exposure within the month prior to birth (see sections 4.4 and 4.8).

Breastfeeding

AUSTELL CITALOPRAM is excreted into the breast milk.

4.7 Effects on ability to drive and use machines

AUSTELL CITALOPRAM may impair performance of skilled tasks. If affected, these patients should not operate machinery or drive.

4.8 Undesirable effects

Tabulated list of adverse reactions

The table below shows all adverse drug reactions (ADRs) observed during reported clinical trials and recorded post-market spontaneous reports with citalopram.

System Organ Class	Frequency		
	Frequent	Less Frequent	Not known
Blood and lymphatic system disorders			Thrombocytopenia
Immune system disorders			Hypersensitivity, anaphylactic reactions, angioedema
Endocrine disorders			Inappropriate ADH secretion
Metabolism and nutrition disorders	Appetite decreased; weight decreased	Increased appetite, weight increased and hyponatraemia	Hypokalaemia
Psychiatric disorders	Agitation, libido decreased, anxiety, nervousness, confusional state, abnormal orgasm (female), abnormal dreams, apathy	Aggression, depersonalisation, hallucination, mania, libido increased	Panic attack, bruxism, restlessness, suicidal ideation and suicidal behaviour.

Nervous system disorders	Somnolence, insomnia, tremor, paraesthesia, dizziness, disturbance in attention, headache, migraine, amnesia	Syncope, grand mal convulsion, dyskinesia, taste disturbance.	Convulsions, serotonin syndrome, extrapyramidal disorders: akathisia and movement disorder
Eye disorders		Mydriasis (which may lead to acute narrow angle glaucoma)	Visual disturbance
Ear and labyrinth disorders	Tinnitus		
Cardiac disorders	Bradycardia, tachycardia	QT-prolongation, ventricular dysrhythmia including torsade de pointes.	
Vascular disorders		Haemorrhage	Oedema and pyrexia, orthostatic hypotension
Respiratory, thoracic and mediastinal disorders	Yawning, rhinitis	Coughing	Epistaxis
Gastrointestinal disorders	Nausea, constipation, diarrhoea, vomiting, dry mouth. dyspepsia, abdominal pain, flatulence, salivary hypersecretion		Gastrointestinal haemorrhage (including rectal haemorrhage)

Hepatobiliary disorders		Hepatitis	Abnormal liver function tests
Skin and subcutaneous tissue disorders	Sweating increased, pruritus	Urticaria, alopecia, purpura and photosensitivity reaction	Ecchymosis and angioedema
Musculoskeletal and connective tissue disorders	Myalgia and arthralgia		
Renal and urinary disorders		Urinary retention	
Reproductive system and breast disorders	Impotence, ejaculation disorder and ejaculation failure	Female: Menorrhagia	Postpartum haemorrhage* Female: Metrorrhagia; Male: Priapism and galactorrhoea

* This event has been reported for the therapeutic class of SSRIs/SNRIs (see sections 4.4 and 4.6).

c. Description of selected adverse reactions

Cases of QT-prolongation and ventricular dysrhythmia including torsade de pointes have been reported during the post-marketing period, predominantly in patients of female gender, with hypokalaemia, or with pre-existing QT prolongation or other cardiac diseases (see section 4.3).

d. Paediatric population

Hostility, suicidal ideation and self-harm have been reported in children (see section 4.3).

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions to SAHPRA via the “**6.04 Adverse Drug Reaction Reporting Form**”, found online under SAHPRA’s publications:

<https://www.sahpra.org.za/Publications/Index/8>

4.9 Overdose

Symptoms of overdose

Tiredness, weakness, sedation, dizziness, tremor, nausea, somnolence and sinus tachycardia (see section 4.8).

Treatment of overdose

There is no specific antidote to AUSTELL CITALOPRAM.

Treatment is symptomatic and supportive and includes the maintenance of a clear airway and monitoring of ECG and vital signs until stable. ECG monitoring is advisable in case of overdose in patients with congestive heart failure/ bradydysrhythmias, in patients using concomitant medications that prolong the QT interval, or in patients with altered metabolism, e.g. liver impairment.

The stomach should be emptied as soon as possible by emesis or gastric lavage. Monitoring of cardiac and vital signs necessary and medical surveillance is advisable for about 24 hours.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and Class: A1.2 Psychoanaleptics (antidepressants)

Pharmacotherapeutic group: antidepressants, selective serotonin reuptake inhibitors ATC Code: N 06 AB 04

Citalopram is a bicyclic phthalane derivative with antidepressant effect. Its effect is linked to the selective inhibition of specific serotonin (5-HT) reuptake. Citalopram, primarily through its (S)-enantiomer, blocks 5-HT

reuptake, leading to potentiation of serotonergic activity in the central nervous system (CNS).

Neither citalopram nor its metabolites have an effect on noradrenaline, dopamine and GABA reuptake. Citalopram also has little or no antidopaminergic, antiadrenergic, antiserotonergic, antihistaminergic or anticholinergic properties.

5.2 Pharmacokinetic properties

Absorption

Oral bioavailability is about 80 % with maximum plasma levels being reached in 4 hours (range 1 to 6 hours).

Distribution

Volume of distribution is about 14 L/kg (range 9 to 17 L/kg). Time to reach steady state concentration is 1 to 2 weeks. Protein binding is about 80 %.

Biotransformation

Elimination half-life is 36 hours (range 28-42 hours). Citalopram undergoes hepatic metabolism primarily involving the cytochrome P450 (CYP3A4) and 2C19 (CYP2C19) isoenzyme and to a small extent cytochrome P450 2D6 (CYP2D6) isoenzyme. The metabolites inhibit the reuptake of serotonin, but are less potent than the parent molecule.

Elimination

Citalopram is excreted mainly via the liver with the remainder via the kidneys (approximately 20 % of which 12 % is unchanged medicine).

Longer half-lives and decreased clearance due to a reduced rate of metabolism have been demonstrated in the elderly.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:

Croscarmellose sodium,
lactose monohydrate,
magnesium stearate,
maize starch,
microcrystalline cellulose (Avicel PH200).

Film-coating:

Hydroxypropyl methylcellulose (E5),
polyethylene glycol 400,
purified talc,
titanium dioxide (EEC no. 171).

6.2 Incompatibilities

Not applicable

6.3 Shelf life

Blister pack (Alu-PVC): 48 months

Bulk pack (HDPE Jar): 36 months

6.4 Special precautions for storage

Store in a dry place at or below 25 °C.

Protect from light.

Keep blister packs in carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container

AUSTELL CITALOPRAM 10 mg

Blister pack (Clear PVDC coated PVC film and Aluminium foil) of 1x14, 2x14, 4x14, 6x14 or 3x10 tablets.

Bulk pack (White HDPE Jars) of 100, 250, 500 or 1000 tablets.

AUSTELL CITALOPRAM 20 mg

Blister pack (Clear PVDC coated PVC film and Aluminium foil) of 1x14, 2x14, 4x14, 6x14 or 3x10 tablets.

Bulk pack (White HDPE Jars) of 100, 250, 500 or 1000 tablets.

AUSTELL CITALOPRAM 40 mg

Blister pack (Clear PVDC coated PVC film and Aluminium foil) of 1x14, 2x14, 4x14, 6x14 or 3x10 tablets.

Bulk pack (White HDPE Jars) of 100, 250, 500 or 1000 tablets.

Not all pack sizes may be marketed.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Austell Pharmaceuticals (Pty) Ltd.

1 Sherborne Road

Parktown

JOHANNESBURG, 2193

South Africa.

Tel: +27 11 611 1400 or +27 860 287 835

8. REGISTRATION NUMBER(S)

AUSTELL CITALOPRAM 10 mg: A39/1.2/0337

AUSTELL CITALOPRAM 20 mg: A39/1.2/0338

AUSTELL CITALOPRAM 40 mg: A39/1.2/0339

**9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE
AUTHORISATION**

Date of registration: 11 August 2006

10. DATE OF REVISION OF THE TEXT

Date of revision: 07 October 2021