SCHEDULING STATUS: S3

1. NAME OF THE MEDICINE

CELEBREX® 100 capsules

CELEBREX® 200 capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 100 mg capsule contains 100 mg celecoxib.

Each 200 mg capsule contains 200 mg celecoxib.

Contains sugar (lactose monohydrate).

Excipients with known effect

Each 100 mg capsule contains 149,7 mg lactose monohydrate.

Each 200 mg capsule contains 49,8 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsules

CELEBREX 100: Hard gelatine capsule (containing white to off-white granulation). White, opaque body with blue ink band containing in white ‘100’; white, opaque cap with blue ink band containing in white ‘7767’. Each blue ink band nearly, but not completely circumscribes the capsule.

CELEBREX 200: Hard gelatine capsule (containing white to off-white granulation). White, opaque body with gold ink band containing in white ‘200’; white, opaque cap with gold ink band containing in white ‘7767’. Each gold ink band nearly, but not completely circumscribes the capsule.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Symptomatic treatment of inflammation and pain in osteoarthritis and rheumatoid arthritis.
- Treatment of pain post dental surgery.

- Treatment of mild to moderate post-operative pain.
- Treatment of mild to moderate musculoskeletal pain.
- Treatment of mild to moderate primary dysmenorrhoea.
- Relief of signs and symptoms of ankylosing spondylitis.

4.2 Posology and method of administration

As the cardiovascular risks of CELEBREX may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used.

Posology

Osteoarthritis

The recommended daily dose is 200 mg, administered as a single dose or as two divided doses. Doses up to 400 mg per day have been studied.

Rheumatoid arthritis

The recommended daily dose is 100 mg or 200 mg twice per day.

Pain post dental surgery

The recommended dose is 100 mg to 200 mg, up to a maximum daily dose of 400 mg. Dosing intervals should not be less than 4 hours.

Mild to moderate post-operative pain

The recommended dose is 200 mg once daily. Some patients may benefit from an additional 200 mg dose.

Mild to moderate musculoskeletal pain

The recommended dose is 200 mg twice daily.

Mild to moderate primary dysmenorrhoea

The recommended dose is 400 mg initially, followed by an additional 200 mg dose if needed on the first day. On subsequent days, the recommended dose is 200 mg twice daily.

Ankylosing spondylitis

The recommended daily dose is 200 mg, administered as a single dose or as 100 mg twice per day. Some patients may benefit from a total daily dose of 400 mg.

Special populations

Elderly

No dosage adjustment is necessary. However, for elderly patients with a lower-than-average body weight (50 kg), it is advisable to initiate therapy at the lowest recommended dose.

Hepatic impairment

No dosage adjustment is necessary in patients with mild hepatic impairment. Introduce CELEBREX at half the-recommended dose in patients with moderate hepatic impairment. For pain post dental surgery, introduce CELEBREX at the lowest recommended dose. There is no clinical experience in patients with severe hepatic impairment (see section 4.3).

Renal impairment

No dosage adjustment is necessary in patients with mild or moderate renal impairment. There is no clinical experience in patients with severe renal impairment (see section 4.3).

CYP2C9 poor metabolisers

Patients who are known or suspected to be CYP2C9 poor metabolisers based on genotyping or previous history/experience with other CYP2C9 substrates should be administered CELEBREX with caution as the risk of dose-dependent adverse effects is increased. Consider reducing the dose to half the lowest recommended dose (see section 5.2).

Paediatric population

CELEBREX has not been studied in subjects under 18 years old.

Method of administration

For oral use.

CELEBREX may be taken with or without food.

4.3 Contraindications

- Hypersensitivity to celecoxib or to any of the excipients of CELEBREX (listed in section 6.1).
- Known sulphonamide hypersensitivity.
- Severe impairment of hepatic function.
- Severe impairment of renal function.
- Asthma, urticaria or allergic-type reactions precipitated by aspirin or other non-steroidal anti-inflammatory drugs (NSAIDs), including other cyclooxygenase 2 (COX-2) specific inhibitors.
- Established ischaemic heart disease and/or cerebrovascular disease (stroke) and peripheral arterial disease.

- Peri-operative analgesia in the setting of coronary artery bypass surgery (CABG).
- Pregnancy.
- In women of childbearing potential unless using an effective method of contraception (see section 4.6). CELEBREX has been shown to cause malformations in the animal species studied (see section 4.6). The potential for human risk in pregnancy is unknown but cannot be excluded.

4.4 Special warnings and precautions for use

CELEBREX may predispose to cardiovascular events, cerebrovascular events, gastrointestinal events or cutaneous reactions which may be fatal.

Safety and efficacy of CELEBREX have not been established for treatment exceeding 12 weeks in osteoarthritis and 24 weeks in rheumatoid arthritis.

Cardiovascular effects

There is insufficient data to assess cardiovascular safety beyond one year of continuous treatment. CELEBREX may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction and stroke, which can be fatal. There appears to be a higher risk for cardiovascular events with higher doses and longer duration of treatment. The shortest duration possible and the lowest effective dose should be used. Caution is advised when CELEBREX is prescribed to patients with cardiovascular risk factors e.g. hypertension, diabetes, smoking and hypercholesterolaemia. Medical practitioners and patients should remain alert for the development of such events, even in the absence of previous cardiovascular symptoms.

Because of its lack of platelet effects, CELEBREX is not a substitute for aspirin for cardiovascular prophylaxis. Therefore, antiplatelet therapies should not be discontinued.

Hypertension

As with all NSAIDs, CELEBREX can lead to the onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of cardiovascular events. Blood pressure should be monitored closely during the initiation of therapy with CELEBREX and throughout the course of therapy.

Gastrointestinal (GI) effects

Upper and lower gastrointestinal perforations, ulcers or bleeds have occurred in patients treated with CELEBREX. Patients most at risk of developing these types of GI complications with NSAIDs are the

elderly, patients with cardiovascular disease, patients using concomitant glucocorticoids, antiplatelet medicines (such as aspirin), or other NSAIDs, patients using alcohol or patients with a prior history of, or active, gastrointestinal disease, such as ulceration, GI bleeding or inflammatory conditions. Most spontaneous reports of fatal gastrointestinal events have been in elderly or debilitated patients.

Serious skin reactions

Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of CELEBREX. Patients appear to be at highest risk for these events early in the course of therapy: the onset of the event occurring in the majority of cases within the first month of treatment. Drug rash with eosinophilia and systemic symptoms (DRESS syndrome) has been reported in patients receiving CELEBREX. CELEBREX should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) has been reported in patients taking NSAIDs such as CELEBREX. Some of these events have been fatal or life-threatening. DRESS typically, although not exclusively, presents with fever, rash, lymphadenopathy, and/or facial swelling. Other clinical manifestations may include hepatitis, nephritis, haematological abnormalities, myocarditis, or myositis. Sometimes symptoms of DRESS may resemble an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its presentation, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, discontinue CELEBREX and evaluate the patient immediately.

Celecoxib contains a sulphonamide moiety. In clinical trials CELEBREX did not induce bronchospasm in patients with asthma. However, CELEBREX has not been evaluated in patients in whom attacks of asthma, urticaria or acute rhinitis have been precipitated by aspirin or NSAIDs. Use in such patients should be avoided until further information is available.

Fluid retention and oedema

As with other medicines known to inhibit prostaglandin synthesis, fluid retention and oedema have been observed in patients taking CELEBREX, therefore CELEBREX should be used with caution in patients with compromised cardiac function, pre-existing oedema and other conditions predisposing to, or

worsened by, fluid retention. Patients with pre-existing congestive heart failure or hypertension should be closely monitored. Caution is also required in patients taking diuretic treatment or otherwise at risk of hypovolaemia.

Renal effects

NSAIDs, including CELEBREX may cause renal toxicity. Clinical trials with CELEBREX have shown renal effects similar to those observed with comparator NSAIDs. Patients at greatest risk for renal toxicity are those with impaired renal function, heart failure, liver dysfunction, and the elderly. Such patients should be carefully monitored while receiving treatment with CELEBREX.

Caution should be used when initiating treatment in patients with dehydration. It is advisable to rehydrate patients first and then start therapy with CELEBREX.

Renal function should be closely monitored in patients with advanced renal disease who are administered CELEBREX.

Hepatic effects

Some cases of severe hepatic reactions, including fulminant hepatitis (some with fatal outcome), liver necrosis and hepatic failure (some with fatal outcome or requiring liver transplant), have been reported with CELEBREX.

A patient with symptoms and/or signs of liver dysfunction, or in whom an abnormal liver function test has occurred, should be monitored carefully for evidence of the development of a more severe hepatic reaction while on therapy with CELEBREX.

CYP2D6 inhibition

CELEBREX inhibits CYP2D6. Although it is not a strong inhibitor of this enzyme, a dose reduction may be necessary for individually dose-titrated medicines that are metabolised by CYP2D6 (see section 4.5).

Anaphylactoid reactions

As with NSAIDs in general, anaphylactoid reactions have occurred in patients exposed to CELEBREX (see section 4.3).

General

By reducing inflammation, CELEBREX may diminish the utility of diagnostic signs, such as fever, in detecting infections.

The concomitant use of CELEBREX and a non-aspirin NSAID should be avoided.

Use with oral anticoagulants

In patients on concurrent therapy with warfarin or similar medicines, serious bleeding events, some of them fatal, have been reported. Because increases in prothrombin time (INR) have been reported, anticoagulant activity should be monitored in patients receiving warfarin/coumarin-type oral anticoagulants after initiating treatment with CELEBREX or changing the dose. Concomitant use of anticoagulants with NSAIDs may increase the risk of bleeding. Caution should be exercised when combining CELEBREX with warfarin or other oral anticoagulants including novel anticoagulants (e.g. apixaban, dabigatran and rivaroxaban).

Lactose intolerance

Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicines and other forms of interaction

General

CELEBREX metabolism is predominantly mediated via cytochrome P450 (CYP) 2C9 in the liver. Co-administration of CELEBREX with medicines that are known to inhibit CYP2C9 should be done with caution.

Concomitant use of inducers of CYP2C9 such as rifampicin, carbamazepine and barbiturates may reduce plasma concentrations of CELEBREX.

In vitro studies indicate that celecoxib, although not a substrate, is an inhibitor of CYP2D6. Therefore, there is a potential for an *in vivo* medicine interaction with medicines that are metabolised by CYP2D6.

Anti-hypertensives

Inhibition of prostaglandins may diminish the effect of anti-hypertensive medicines including angiotensin converting enzyme (ACE) inhibitors, angiotensin II receptor antagonists, diuretics and beta-blockers. The risk of acute renal insufficiency, which is usually reversible, may be increased in some patients with compromised renal function (e.g. patients on diuretics or elderly patients) when ACE-inhibitors, angiotensin II receptor antagonists and/or diuretics are combined with NSAIDs, including CELEBREX. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated, and consideration should be given to monitoring of renal function after initiation of concomitant therapy, and periodically thereafter.

In a 28-day clinical study in patients with lisinopril-controlled Stage I and II hypertension, administration of CELEBREX 200 mg twice daily resulted in no clinically significant increases, when compared to placebo treatment, in mean daily systolic or diastolic blood pressure as determined using 24-hour ambulatory blood pressure monitoring. Among patients treated with CELEBREX 200 mg twice daily, 48 % were considered unresponsive to lisinopril at the final clinic visit (defined as either cuff diastolic blood pressure > 90 mmHg or cuff diastolic blood pressure increased > 10 % compared to baseline), compared to 27 % of patients treated with placebo; this difference was statistically significant.

Aspirin

CELEBREX can be used with low dose aspirin. However, concomitant administration of aspirin with CELEBREX may result in an increased rate of GI ulceration or other complications, compared to use of CELEBREX alone. Because of its lack of platelet effects, CELEBREX is not a substitute for aspirin for cardiovascular prophylaxis. There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious cardiovascular thromboembolic events associated with CELEBREX.

Ciclosporin

Co-administration of NSAIDs and ciclosporin may increase the nephrotoxic effect of ciclosporin.

Fluconazole

Concomitant administration of fluconazole at 200 mg once daily resulted in a two-fold increase in CELEBREX plasma concentration. This increase is due to the inhibition of CELEBREX metabolism via CYP2C9 by fluconazole. CELEBREX should be introduced at half the recommended dose in patients receiving the CYP2C9 inhibitor fluconazole.

Dextromethorphan and metoprolol

Concomitant administration of CELEBREX 200 mg twice daily resulted in 2,6-fold and 1,5-fold increases in plasma concentrations of dextromethorphan and metoprolol (CYP2D6 substrates), respectively. These increases are due to CELEBREX inhibition of the CYP2D6 substrate metabolism.

Diuretics

Clinical studies, as well as post-marketing observations, have shown that NSAIDs can reduce the natriuretic effect of furosemide and thiazides in some patients. This response has been attributed to inhibition of renal prostaglandin synthesis.

Glibenclamide

CELEBREX does not affect the pharmacokinetics of glibenclamide to a clinically relevant extent.

Ketoconazole and antacids

Ketoconazole or antacids have not been observed to affect the pharmacokinetics of CELEBREX.

Lithium

In a study conducted in healthy subjects, mean steady-state lithium plasma levels increased approximately 17 % in subjects receiving lithium 450 mg twice daily with CELEBREX 200 mg twice daily as compared to subjects receiving lithium alone. Patients on lithium treatment should be closely monitored when CELEBREX is introduced or withdrawn.

Methotrexate

In an interaction study of rheumatoid arthritis patients taking methotrexate, CELEBREX did not have a significant effect on the pharmacokinetics of methotrexate.

Other medicines

In specific studies in healthy volunteers with other medicines metabolised by CYP2C9, CELEBREX was found to produce no clinically significant pharmacokinetic interaction with phenytoin or tolbutamide.

Oral contraceptives

In an interaction study, CELEBREX had no clinically relevant effects on the pharmacokinetics of a prototype combination oral contraceptive (1 mg norethindrone/0,035 mg ethinyl estradiol).

Warfarin

In patients on concurrent therapy with warfarin, increases in prothrombin time (INR) have been reported (see section 4.4).

4.6 Fertility, pregnancy and lactation

Fertility

Based on the mechanism of action, the use of NSAIDs, including CELEBREX, may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women.

Pregnancy

Studies in animals have shown reproductive toxicity. Inhibition of prostaglandin synthesis might adversely affect pregnancy. Data from epidemiological studies suggest an increased risk of spontaneous abortion after use of prostaglandin synthesis inhibitors in early pregnancy. CELEBREX, as with other medicines inhibiting prostaglandin synthesis, may cause uterine inertia and premature closure of the ductus arteriosus and should be avoided during pregnancy.

During the second or third trimester of pregnancy, NSAIDs including CELEBREX may cause foetal renal dysfunction which may result in reduction of amniotic fluid volume or oligohydramnios in severe cases. Such effects may occur shortly after treatment initiation and are usually reversible.

Breastfeeding

CELEBREX is excreted in the milk of lactating rats at concentrations similar to those in plasma. Limited data indicate that CELEBREX is excreted in breast milk and therefore should not be used during lactation.

4.7 Effects on ability to drive and use machines

The effect of CELEBREX on ability to drive or use machinery has not been studied but based on its pharmacodynamic properties and overall safety profile it is unlikely to have an effect.

4.8 Undesirable effects

Tabulated summary of adverse reactions

The following side effects have been reported in patients on CELEBREX treatment. Incidence rates are categorised as follows: Very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000).

MedDRA System Organ Class	**Frequency**	**Undesirable effects**
Infections and infestations	Common	Bronchitis, pharyngitis, rhinitis, sinusitis, upper respiratory tract infection urinary tract infection
Blood and lymphatic system disorders	Uncommon	Anaemia, thrombocytopenia
Immune system disorders	Common	Allergy aggravated
	Uncommon	Hypersensitivity
	Rare	Angioedema
Psychiatric disorders	Common	Insomnia
	Uncommon	Anxiety
	Rare	Confusion
Nervous system disorders	Common	Dizziness, hypertonia
	Uncommon	Somnolence

Eye disorders	Uncommon	Blurred vision
Ear and labyrinth disorders	Uncommon	Tinnitus
Cardiac disorders	Uncommon	Arrhythmia, palpitations, tachycardia
	Rare	Congestive heart failure
Vascular disorders	Common	Hypertension (including aggravated hypertension)
	Uncommon	Flushing
Respiratory, thoracic and mediastinal disorders	Common	Cough
Gastrointestinal disorders	Common	Vomiting, abdominal pain, diarrhoea, dyspepsia, flatulence, tooth disorder
	Uncommon	Gastric ulcer
	Rare	Pancreatitis, duodenal ulcer, oesophageal ulcer, intestinal perforation
Hepatobiliary disorders	Uncommon	Increased hepatic enzyme (including increased SGOT and SGPT)
Skin and subcutaneous tissue disorders	Common	Rash, pruritus
	Uncommon	Alopecia, urticaria, ecchymosis
	Rare	Angioedema, bullous dermatitis
General disorders and administration site conditions	Common	Peripheral oedema, influenza-like illness
	Uncommon	Face oedema
Injury, poisoning and procedural complications	Common	Accidental injury

Post-marketing experience

Reactions from post-marketing experience include the following:

MedDRA System Organ Class	**Undesirable effects**
Immune system disorders	Anaphylactic reaction
Psychiatric disorders	Hallucination
Nervous system disorders	Intracranial haemorrhage, ageusia, anosmia, aseptic meningitis, cerebrovascular incident (stroke)

Eye disorders	Conjunctivitis
Cardiac disorders	Myocardial infarction, cardiovascular thrombotic events
Vascular disorders	Vasculitis
Respiratory, thoracic and mediastinal disorders	Pulmonary embolism, pneumonitis
Gastrointestinal disorders	Gastrointestinal haemorrhage
Hepatobiliary disorders	Hepatitis, hepatic failure, fulminant hepatitis, hepatic necrosis, cholestasis, cholestatic hepatitis, jaundice
Skin and subcutaneous tissue disorders	Photosensitivity reaction, skin exfoliation (including erythema multiforme and Stevens-Johnson syndrome), toxic epidermal necrolysis, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) (see section 4.4), acute generalised exanthematous pustulosis (AGEP), exfoliative dermatitis
Renal and urinary disorders	Acute renal failure, tubulointerstitial nephritis, hyponatraemia, nephrotic syndrome, glomerulonephritis minimal lesion
Reproductive system and breast disorders	Menstrual disorder, female infertility (decreased female fertility)
General disorders and administration site conditions	Chest pain

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. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8.

4.9 Overdose

There is no clinical experience of overdose. Single doses up to 1 200 mg and multiple doses up to 1 200 mg twice daily have been administered to healthy subjects without clinically significant adverse effects. In the event of suspected overdose, appropriate supportive medical care should be provided. Dialysis is unlikely to be an efficient method of medicine removal.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 3.1 Antirheumatics (anti-inflammatory agents)

Mechanism of action

Celecoxib is a non-steroidal anti-inflammatory drug (NSAID) acting as a specific cyclooxygenase 2 inhibitor (SCI). Cyclooxygenase 2 (COX-2) is induced in response to inflammatory stimuli. This leads to the synthesis and accumulation of inflammatory prostanoids, in particular prostaglandin E2, causing inflammation, oedema and pain. Celecoxib acts as an anti-inflammatory, analgesic and anti-pyretic medicine by blocking the production of inflammatory prostanoids via COX-2 inhibition.

In vivo and *ex vivo* studies show that celecoxib has a very low affinity for the constitutively expressed cyclooxygenase 1 enzyme (COX-1).

5.2 Pharmacokinetic properties

Absorption

When given under fasting conditions celecoxib reaches peak plasma concentrations after approximately 2 – 3 hours. Dosing with food (high fat meal) delays absorption, resulting in a T_{max} of about 4 hours, and increases bioavailability by about 20 %.

Distribution

Plasma protein binding, which is concentration independent, is about 97 % at therapeutic plasma concentrations and celecoxib is not preferentially bound to erythrocytes in the blood.

Biotransformation

Celecoxib metabolism is primarily mediated via cytochrome P450 2C9. Three metabolites, inactive as COX-1 or COX-2 inhibitors, have been identified in human plasma – a primary alcohol, the corresponding carboxylic acid and its glucuronide conjugate.

Cytochrome P450 2C9 activity is reduced in individuals with genetic polymorphisms that lead to reduced enzyme activity, such as those homozygous for the CYP2C9*3 polymorphism.

In a pharmacokinetic study of celecoxib 200 mg administered once daily in healthy volunteers, genotyped as either CYP2C9*1/*1, CYP2C9*1/*3, or CYP2C9*3/*3, the median C_{max} and AUC_{0-24} of celecoxib on day 7 were approximately 4-fold and 7-fold, respectively, in subjects genotyped as

CYP2C9*3/*3 compared to other genotypes. In three separate single dose studies, involving a total of 5 subjects genotyped as CYP2C9*3/*3, single-dose AUC_{0-24} increased by approximately 3-fold compared to normal metabolisers. It is estimated that the frequency of the homozygous *3/*3 genotype is 0.3 – 1.0 % among different ethnic groups.

Patients who are known or suspected to be CYP2C9 poor metabolisers based on previous history/experience with other CYP2C9 substrates should be administered celecoxib with caution (see section 4.2).

Elimination

Elimination of celecoxib is mostly by hepatic metabolism with less than 1 % of the dose excreted unchanged in urine. After multiple dosing, elimination half-life is 8 – 12 hours and the rate of clearance about 500 mL/min. With multiple dosing, steady state plasma concentrations are reached before day 5. The intersubject variability on the main pharmacokinetic parameters (AUC, C_{max}, elimination half-life) is about 30 %. The mean steady state volume of distribution is about 500 L/70 kg in young healthy adults after a single 200 mg dose, indicating wide distribution of celecoxib into the tissues. Pre-clinical studies indicate that the medicine crosses the blood/brain barrier.

Linearity/non-linearity

Celecoxib exhibits linear and dose proportional pharmacokinetics over the therapeutic dose range.

Special populations

Elderly

In the population > 65 years there is a two-fold increase in mean C_{max} and AUC for celecoxib. This is a predominantly weight-related rather than age-related change – celecoxib levels being higher in lower weight individuals and consequently higher in the elderly population who are generally of lower mean weight than the younger population. Therefore, elderly females tend to have slightly higher medicine plasma concentrations than elderly males.

Hepatic impairment

Plasma concentrations of celecoxib in patients with mild hepatic impairment are not significantly different from those of age and sex matched controls. In patients with moderate hepatic impairment celecoxib plasma concentrations are about twice those of matched controls. Patients with severe hepatic impairment have not been studied but can be expected to show accumulation of the parent medicine as the main route of metabolism is via the liver.

Renal impairment

In elderly volunteers with age-related reductions in glomerular filtration rate (GFR) (mean GFR > 65 mL/min 1,73 m^2) and in patients with chronic stable renal insufficiency (GFR 35 – 60 mL/min/1,73 m^2), celecoxib pharmacokinetics were comparable to those seen in patients with normal renal function. No significant relationship was found between serum creatinine (or creatinine clearance) and celecoxib clearance.

Renal effects

At the present time the relative roles of COX-1 and COX-2 in renal physiology is incompletely understood. Celecoxib reduces the urinary excretion of PGE2 and 6-keto-PGF1∝ (a prostacyclin metabolite) but leaves serum thromboxane B2 (TXB2) and urinary excretion of 11-dehydro-TXB2, a thromboxane metabolite (both COX-1 products), unaffected. Specific studies have shown that celecoxib produces no decrease in GFR in the elderly or those with chronic renal insufficiency. These studies have also shown transient reductions in fractional excretion of sodium.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content

Croscarmellose sodium

Lactose monohydrate

Magnesium stearate

Povidone

Sodium lauryl sulphate

Capsule shells

Gelatine

Titanium dioxide

Printing ink

Butyl alcohol (E1013200)

Dehydrated alcohol (E1034800)

FD&C Blue #2 Aluminium Lake (E132) (100 mg)

Isopropyl alcohol

Propylene glycol

Shellac

Strong ammonia solution

Yellow ferric oxide (E172) (200 mg)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

CELEBREX 100: Blister packs of 60 capsules.

CELEBREX 200: Blister packs of 10, 15 or 30 capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Viatris Healthcare (Pty) Ltd

4 Brewery Street

Isando

Gauteng, 1609

Tel.: +27(011) 451 1300 / +27(071) 281 2503 (24 hours)

Manufacturer: Viatris Pharmaceuticals LLC, Vega Baja, Puerto Rico

8. REGISTRATION NUMBERS

CELEBREX 100: 33/3.1/0332

CELEBREX 200: 33/3.1/0333

9. DATE OF FIRST AUTHORISATION

28 January 2000

10. DATE OF REVISION OF THE TEXT

13 February 2022

BOTSWANA: S2

CELEBREX 100 – Reg. No.: BOT0801379

CELEBREX 200 – Reg. No.: BOT0801377

NAMIBIA: NS2

CELEBREX 100 – Reg. No.: 04/3.1/0721

CELEBREX 200 – Reg. No.: 04/3.1/0722