NEW ZEALAND DATA SHEET

1. PRODUCT NAME

PONSTAN® Mefenamic acid 250 mg capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

PONSTAN capsules contain the active ingredient mefenamic acid 250 mg/capsule.

Excipients with known effects

- Lactose monohydrate

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

PONSTAN capsules have an opaque aqua blue cap and opaque ivory body with “PARKE DAVIS” printed in black on both the body and cap.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PONSTAN is indicated for the treatment of primary dysmenorrhoea, dysfunctional uterine bleeding and pain or menorrhagia due to Intrauterine Contraceptive Devices (IUCDs).

It is also effective in pain of miscellaneous origin, including arthritic, soft tissue and dental pain.

PONSTAN has demonstrated antipyretic action in certain febrile conditions.

4.2 Dose and method of administration

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms.

Patients on long-term treatment should be reviewed regularly with regards to efficacy, risk factors and ongoing need for treatment.

For use in pregnancy: see sections 4.3 and 4.6.

Dysmenorrhoea

2 capsules (500 mg) three times daily with meals from the onset of pain and continued for the usual duration of pain.

Menorrhagia

2 capsules (500 mg) three times daily with meals and from the onset of menses and continued according to the judgement of the physician. Therapy should not be continued for more than 7 days except on the advice of a physician.

Other Indications

2 capsules (500 mg) three times daily, with meals.

Use in the Elderly and Renal Dysfunction

Caution is required with dosage in the elderly and patients with renal dysfunction (see section 4.4).

Use in Children

PONSTAN is not recommended for children under 14 years of age.

4.3 Contraindications

Patients showing evidence of chronic inflammation and/or active ulceration of either the upper or lower gastrointestinal tract and patients with pre-existing renal disease.

Patients in whom aspirin and/or other non-steroidal anti-inflammatory drugs (NSAIDs) have induced symptoms of bronchospasm, allergic rhinitis or urticaria because the potential exists for cross-sensitivity.

Patients with impaired renal function.

Patients with severe hepatic impairment.

Patients previously experiencing diarrhoea on taking this drug.

Patients who have previously exhibited hypersensitivity to mefenamic acid or any of the components of PONSTAN (see section 6.1).

Patients with severe heart failure.

Treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.

Children under 14 years of age.

Patients in the third trimester of pregnancy.

4.4 Special warnings and precautions for use

Should pain not be restricted directly to the time of menses, further investigations to exclude the possibility of pelvic disease are indicated prior to prescribing the drug.

PONSTAN is indicated for primary menorrhagia; therefore, secondary causes of menorrhagia (e.g. endometriosis) should be excluded before prescribing the drug for this indication.

The use of PONSTAN with concomitant systemic non-aspirin NSAIDs, including cyclooxygenase-2 (COX-2) inhibitors, should be avoided. Concomitant use with one or more systemic NSAIDs may increase frequency of gastrointestinal ulcers and bleeding.

Cardiovascular Effects

Cardiovascular Thrombotic Events: NSAIDs may cause an increased risk of serious cardiovascular (CV) thrombotic events, myocardial infarction and stroke, which can be fatal. This risk may increase with dose or duration of use. The relative increase of this risk appears to be similar in those with or without known CV disease or CV risk factors. However, patients with CV disease, history of atherosclerotic CV disease or CV risk factors may also be at greater risk in terms of absolute incidence, due to their increased rate at baseline. To minimise the potential risk for an adverse CV event in patients treated with mefenamic acid, especially in patients with CV risk factors, the lowest effective dose should be used for the shortest duration possible. Physicians and patients should remain alert for the development of such events, even in the absence of previous CV symptoms. Patients should be informed about the signs and/or symptoms of serious CV toxicity and the steps to take if they occur (see section 4.3).

There is no consistent evidence that concurrent use of aspirin mitigates the increased risk of serious CV thrombotic events associated with NSAID use.

Hypertension: NSAIDs may lead to the onset of new hypertension or worsening of pre-existing hypertension and patients taking anti-hypertensives with NSAIDs may have an impaired anti-hypertensive response. Caution is advised when prescribing NSAIDs to patients with hypertension. Blood pressure should be monitored closely during initiation of NSAID treatment and at regular intervals throughout the course of therapy.

Heart Failure: Fluid retention and oedema have been observed in some patients taking NSAIDs, including mefenamic acid. Therefore, PONSTAN should be used with caution in patients with compromised cardiac function and other conditions predisposing to, or worsened by, fluid retention. Patients with pre-existing heart failure or hypertension should be closely monitored.

Gastrointestinal Effects

NSAIDs, including mefenamic acid, can cause serious, potentially fatal gastrointestinal (GI) adverse events including inflammation, bleeding, ulceration and perforation of the stomach, small intestine or large intestine. The frequency of such events may increase with dose or duration of use, but can occur at any time without warning.

Upper GI ulcers, gross bleeding or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3-6 months and in about 2-4% of patients treated for one year. These trends

continue with longer duration of use, increasing the likelihood of developing a serious GI event at some time during the course of therapy. However, even short-term therapy is not without risk.

Patients most at risk of developing GI complications with NSAIDs are the elderly; patients with CV disease; patients using concomitant corticosteroids, anti-platelet drugs (such as aspirin), or selective serotonin reuptake inhibitors (SSRIs); patients with a history of, or active, GI disease (such as ulceration, bleeding or inflammatory conditions); and patients ingesting alcohol or with a history of smoking and alcoholism. Mefenamic acid should be used with caution in these patients (see section 4.3). When GI bleeding or ulceration occurs in patients receiving PONSTAN, the drug should be withdrawn immediately. Physicians should inform patients about the signs and/or symptoms of serious GI toxicity and what steps to take if they occur.

If diarrhoea occurs, PONSTAN should be promptly discontinued. Symptoms may recur in certain patients following subsequent exposure.

Severe Skin Reactions

NSAIDs may very rarely cause serious cutaneous adverse events such as drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome (see Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome), exfoliative dermatitis, toxic epidermal necrolysis (TEN), Stevens-Johnson syndrome (SJS), and generalised bullous fixed drug eruption (GBFDE) which can be fatal and occur without warning. These serious adverse events are idiosyncratic and are independent of dose or duration of use. Patients should be advised of the signs and symptoms of serious skin reactions and to consult their doctor at the first appearance of a skin rash, mucosal lesion or any other sign of hypersensitivity. If this occurs, the drug should be promptly discontinued.

PONSTAN may cause an exacerbation of chronic urticaria in patients with this disease.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) Syndrome

DRESS syndrome has been reported in patients taking NSAIDs. Some of these events have been fatal or life-threatening. DRESS syndrome 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 syndrome 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 the NSAID and evaluate the patient immediately.

Renal Effects

As with other NSAIDs, long-term administration of PONSTAN to animals has resulted in renal papillary necrosis and other abnormal renal pathology. In humans, there have been reports of acute interstitial nephritis with haematuria, proteinuria, glomerulitis, papillary necrosis and occasionally nephrotic syndrome.

A second form of renal toxicity has been seen in patients with pre-renal conditions leading to a reduction in renal blood flow or blood volume, where the renal prostaglandins have a supportive role in the maintenance of renal perfusion. In these patients, administration of an NSAID may cause a dose-dependent reduction in prostaglandin formation and may precipitate overt renal decomposition. Patients at greatest risk of this reaction are those with impaired renal function, heart failure, liver dysfunction, nephrotic syndrome, those taking diuretics and the elderly. Such patients should be carefully monitored while receiving PONSTAN.

Discontinuation of NSAID therapy is typically followed by recovery to the pre-treatment state. Since PONSTAN is eliminated primarily by the kidneys, the drug should not be administered to patients with significantly impaired renal functions (see section 4.3).

Renal function should be checked periodically.

Hepatic Effects

PONSTAN should be used with caution in patients with hepatic impairment.

As with other NSAIDs, borderline elevations of liver function tests may occur in up to 15% of patients. These elevations may progress, may remain essentially unchanged, or may be transient with continued therapy. Meaningful (3 times the upper limit of normal) elevations of ALT or AST occurred in controlled clinical trials in less than 1% of patients.

Physicians and patients should remain alert for hepatotoxicity. Patients should be informed about the signs and/or symptoms of hepatotoxicity. A patient with symptoms and/or signs suggesting liver dysfunction (e.g. nausea, fatigue, lethargy, pruritis, jaundice, abdominal tenderness in the right upper quadrant and “flu-like” symptoms), or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of a more severe hepatic reaction while on therapy with mefenamic acid.

Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with other NSAIDs. Although such reactions are rare, if abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g. eosinophilia, rash, etc.), PONSTAN should be discontinued.

Haematologic Effects

PONSTAN 500 mg and aspirin 650 mg, four times a day, both caused significant further lowering of the prothrombin concentration (PONSTAN 3.48% and aspirin 2.75%) in patients in whom the concentration has been initially lowered by anticoagulant therapy. Caution should therefore be exercised in administering PONSTAN to patients on anticoagulant therapy, such as warfarin, and should not be given when prothrombin concentration is in the range of 10% to 20% of normal. Careful monitoring of blood coagulation factors is recommended (see section 4.5).

Use with Oral Anticoagulants

The concomitant use of NSAIDs, including PONSTAN, with oral anticoagulants increases the risk of GI and non-GI bleeding and should be given with caution. Oral anticoagulants include warfarin/coumarin-type and novel oral anticoagulants (e.g. apixaban, dabigatran, rivaroxaban).

Anticoagulation/INR should be monitored in patients taking a warfarin/coumarin-type anticoagulant (see section 4.5).

Other Effects

PONSTAN should be used with caution in known asthmatics.

As no data presently exist concerning the effect of PONSTAN, if any, on the efficacy of intrauterine contraceptive devices, physicians should be alert to the possibility of a reduction in contraceptive efficacy in women with an IUCD taking PONSTAN.

Paediatric Use

Safety and effectiveness in children below the age of 14 years have not been established.

Effects on Laboratory Tests

A false positive reaction for urinary bile, using the diazo tablet test, may result after PONSTAN administration. If biliuria is suspected, other diagnostic procedures, such as the Harrison spot test, should be performed.

4.5 Interaction with other medicines and other forms of interaction

Aspirin

Mefenamic acid interferes with the anti-platelet effect of low-dose aspirin, and thus may interfere with aspirin's prophylactic treatment of CV disease.

Anticoagulants

The concurrent use of NSAIDs and warfarin has been associated with severe, sometimes fatal, haemorrhage.

Mefenamic acid, like other non-steroidal anti-inflammatory agents, can inhibit platelet aggregation and may prolong prothrombin time in patients on warfarin therapy. Mefenamic acid has been shown to displace warfarin from protein binding sites and may enhance the response to oral anticoagulants.

NSAIDs, such as PONSTAN, should be used in combination with warfarin, only if absolutely necessary. Concurrent administration of PONSTAN with oral anticoagulant drugs requires frequent prothrombin time monitoring (see section 4.4).

Anti-hypertensives

NSAIDs, such as mefenamic acid, can reduce the efficacy of anti-hypertensive drugs including diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II antagonists (AIIAs) and beta-blockers.

In patients with impaired renal function (e.g. dehydrated patients or elderly patients with compromised renal function), the co-administration of an ACE inhibitor or an AIIA and/or diuretics with a cyclooxygenase inhibitor can increase the deterioration of the renal function, including the possibility of acute renal failure, which is usually reversible. The occurrence of these interactions should be considered in patients taking mefenamic acid with an ACE inhibitor or an AIIA and/or diuretics.

Therefore, the concomitant administration of these drugs should be done with caution, especially in elderly patients. Patients should be adequately hydrated and the need to monitor renal function should be assessed before, and periodically during, concomitant treatment.

Corticosteroids

Concurrent use with NSAIDs may increase the risk of gastrointestinal ulceration or bleeding.

Cyclosporin or Tacrolimus

Concomitant administration with NSAIDs increases the risk of nephrotoxicity.

Hypoglycaemic Agents

There have been reports of changes in the effects of oral hypoglycaemic agents in the presence of NSAIDs. Therefore, mefenamic acid should be administered with caution in patients receiving insulin or oral hypoglycaemic agents.

Lithium

Mefenamic acid has produced an elevation of plasma lithium levels and a reduction in renal lithium clearance. Thus, when mefenamic acid and lithium are administered concurrently, patients should be observed carefully for signs of lithium toxicity.

Methotrexate

Caution is advised when methotrexate is administered concurrently with NSAIDs, including mefenamic acid, because NSAID administration may result in increased plasma levels of methotrexate, especially in patients receiving high doses of methotrexate.

4.6 Fertility, pregnancy and lactation

Pregnancy - Category C

PONSTAN is contraindicated in the third trimester of pregnancy.

PONSTAN should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus. If there is a compelling need for NSAID treatment during the first or second trimester, limit use to the lowest effective dose and shortest duration possible.

Data from epidemiological studies suggest an increased risk of miscarriage and congenital malformation associated with NSAID use in early pregnancy.

NSAIDs given during the third trimester of pregnancy may cause closure of the fetal ductus arteriosus, fetal renal impairment, inhibition of platelet aggregation, and delay labour and birth. It is not known if mefenamic acid or its metabolites cross the placenta. However, because of the effects of drugs in this class (i.e. inhibitors of prostaglandin synthesis) on the fetal CV system (i.e. premature closure of the ductus arteriosus), the use of mefenamic acid in pregnant women is not recommended and is therefore contraindicated during the third trimester of pregnancy, including the last few days before expected birth.

Oligohydramnios and Neonatal Renal Impairment

Use of NSAIDs in the second or third trimester may cause fetal renal dysfunction leading to oligohydramnios and, in some cases, neonatal renal impairment. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. Oligohydramnios is often, but not always, reversible with treatment discontinuation. Complications of prolonged oligohydramnios may, for example, include limb contractures and delayed lung maturation. In some post-marketing cases of impaired neonatal renal function, invasive procedures such as exchange transfusion or dialysis were required. Consider ultrasound monitoring of amniotic fluid if treatment extends beyond 48 hours. Discontinue treatment with NSAIDs if oligohydramnios occurs.

Mefenamic acid inhibits prostaglandin synthesis which may result in prolongation of pregnancy and interference with labour when administered late in the pregnancy. Women on mefenamic acid therapy should consult their physician if they decide to become pregnant.

The inhibition of prostaglandin synthesis by NSAIDs may adversely affect pregnancy. Epidemiological studies suggest an increased risk of spontaneous abortion after use of prostaglandin synthesis inhibitors in early pregnancy. In animals, administration of prostaglandin synthesis inhibitors has been shown to result in increased pre- and post-implantation loss.

Breast-feeding

Trace amounts of PONSTAN may be present in breast milk and transmitted to the nursing infant. Thus, PONSTAN should not be taken by the nursing mother because of the effects of this class of drugs on the infant cardiovascular system.

Fertility

Based on the mechanism of action, the use of NSAIDs may delay or prevent rupture of ovarian follicles, which has been associated with reversible infertility in some women. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawal of NSAIDs, including PONSTAN, should be considered.

4.7 Effects on ability to drive and use machines

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration. However, adverse effects of PONSTAN include dizziness, drowsiness and blurred vision which could affect the ability to drive or use machines (see section 4.8).

4.8 Undesirable effects

Gastrointestinal Disorders

The most frequently reported adverse effects associated with the use of PONSTAN involve the gastrointestinal tract. In controlled studies for up to eight months, the following disturbances were reported in decreasing order of frequency: diarrhoea (approximately 5% of patients), nausea with or without vomiting, other gastrointestinal symptoms and abdominal pain. In certain patients, the diarrhoea was of sufficient severity to require discontinuation of the medication. Diarrhoea is usually dose related. It generally subsides on reduction of dosage and rapidly disappears on termination of therapy.

Other less frequently reported gastrointestinal effects were anorexia, cholestatic jaundice, colitis, enterocolitis, mild hepatic toxicity, hepatitis, hepatorenal syndrome, pyrosis, pancreatitis, steatorrhoea, flatulence, constipation, gastrointestinal inflammation, gastrointestinal ulceration (with and without haemorrhage) and gastrointestinal perforation.

Blood and Lymphatic System

Cases of auto-immune haemolytic anaemia have been associated with the continuous administration of PONSTAN for 12 months or longer. In such cases the Coombs test results are positive with evidence of both accelerated RBC production and RBC destruction. The process is reversible upon termination of PONSTAN administration.

Decreases in haematocrit have been noted in 2% to 5% of patients and primarily in those who have received prolonged therapy. Leukopenia, eosinophilia, thrombocytopenia purpura, agranulocytosis, pancytopenia, aplastic anaemia, bone marrow hypoplasia and platelet aggregation inhibition have also been reported.

Immune System

Anaphylaxis.

Metabolism and Nutrition

Glucose intolerance in diabetic patients, hyponatraemia and fluid retention.

Psychiatric Disorders

Nervousness.

Nervous System

Aseptic meningitis, convulsions, drowsiness, dizziness, headache, blurred vision and insomnia.

Eye and Ear Disorders

Eye irritation, reversible loss of colour vision and ear pain.

Cardiovascular System

Hypotension, hypertension and palpitations.

Respiratory and Thoracic System

Asthma and dyspnoea.

Skin and Subcutaneous Tissue Disorders

Angioedema, oedema of the larynx, erythema multiforme, perspiration, Lyell's syndrome (toxic epidermal necrolysis), Stevens-Johnson syndrome, dermatitis exfoliative, pruritus, urticaria, rash, facial oedema, and generalised bullous fixed drug eruption (GBFDE).

Renal and Urinary Disorders

As with other NSAIDs, renal failure including papillary necrosis has been reported. In elderly patients, renal failure has occurred after taking PONSTAN for 2 to 6 weeks. The renal damage may not be completely reversible. Haematuria, dysuria, tubulointerstitial nephritis, glomerulonephritis and nephrotic syndrome have also been reported.

General Disorders and Administration Site Conditions

Oedema.

Investigations

Urobilinogen urine (false-positive) and liver function test abnormal.

Post-marketing experience

In post-marketing experience, the following adverse effects have occurred from NSAID use that cannot be excluded as a class-effect:

Pregnancy, Puerperium and Perinatal Conditions

Oligohydramnios, ductus arteriosus premature closure, prolonged labour, prolonged pregnancy, neonatal renal impairment.

Skin and Subcutaneous Tissue Disorders

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome.

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 https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

Signs and Symptoms

Symptoms of overdosage are related to the amount of drug ingested and range from gastrointestinal discomfort and diarrhoea to seizures, acute renal failure, confusional state, vertigo, hallucination, coma and death. Plasma levels of up to 210 mcg/mL (therapeutic range 1 to 10 mcg/mL) have been reported resulting in repeated generalised convulsions, but are not generally useful for evaluation and management of overdosage.

Treatment

There is no specific antidote for mefenamic acid overdose. Treatment is symptomatic and supportive, including fluid replacement and IV access especially to patients who are dehydrated or unable to ingest adequate fluids. Avoiding intravascular fluid depletion will help prevent development of renal failure.

In cases of severe toxicity, activated charcoal may reduce absorption of the drug if given within one to two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via nasogastric tube ensuring that the airway is protected.

In clinically severe overdoses, full blood count, electrolytes, glucose, renal function, liver function tests, arterial blood gases and coagulation studies should be monitored for abnormalities.

Because mefenamic acid and its metabolites are firmly bound to plasma proteins, haemodialysis, haemoperfusion and peritoneal dialysis may be of little value.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

PONSTAN has demonstrated analgesic, anti-inflammatory and antipyretic properties in human clinical studies and in classical animal test systems. These effects may be due to PONSTAN's dual

action on prostaglandins. It inhibits the enzymes of prostaglandin synthetase and also antagonises the actions of prostaglandin at the receptor sites. These effects may also be responsible for its effectiveness in the treatment of primary dysmenorrhoea. The pain of primary dysmenorrhoea is thought to be due to increased abnormal uterine activity and uterine ischaemia, probably induced by release of $PGF_{2\alpha}$ or due to increase in the ratio of $PGF_{2\alpha}$: PGE_2. Prostaglandins are also believed to be responsible, at least in some part, for the symptoms of menorrhagia. The dual mode of action of PONSTAN offers significant advantages in certain gynaecological indications over other non-steroidal anti-inflammatory agents which merely inhibit prostaglandin synthesis.

5.2 Pharmacokinetic properties

Absorption

Single and multiple studies have shown that PONSTAN usually reaches peak plasma levels 2 to 4 hours after oral administration with a half-life of 2 hours.

Distribution

Mefenamic acid and its metabolites are firmly bound to plasma proteins.

Biotransformation

Mefenamic acid metabolism is predominantly mediated via cytochrome P450 CYP 2C9 in the liver. Patients who are known or suspected to be poor CYP2C9 metabolisers based on previous history/experience with other CYP2C9 substrates, should be administered mefenamic acid with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.

Two distinct metabolic products, one a hydroxymethyl derivative and the other a carboxy derivative, have been identified in both plasma and urine. Mefenamic acid and its two metabolic derivatives become conjugated with glucuronic acid through an ester linkage which is alkali labile and are excreted principally in the urine, but also to some extent in the bile and faeces.

Elimination

Following a single dose, 67% of the total dose is excreted in the urine as unchanged drug or as one of the two metabolites. 20% to 25% of the dose is excreted in the faeces during the first three days.

5.3 Preclinical safety data

Carcinogenicity

None stated.

Genotoxicity

None stated.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Lactose monohydrate
- Titanium dioxide
- Gelatin
- Brilliant blue FCF
- Iron oxide yellow
- Carbon black

6.2 Incompatibilities

None stated.

6.3 Shelf life

Prescription Medicine – 30 months for PVC/Al blister and 36 months for plastic HDPE bottle.

Pharmacy Only Medicine – 36 months.

6.4 Special precautions for storage

Store below 30 °C.

6.5 Nature and contents of container

Prescription Medicine – PVC/Al blister and plastic HDPE bottle packs of 50 capsules.

Pharmacy Only Medicine – PVC/Al blister packs of 20 capsules.

Not all presentations may be marketed.

6.6 Special precautions for disposal and other handling

Any unused medicine or waste material should be disposed of in accordance with local requirements.

7. MEDICINE SCHEDULE

Packs of 50 capsules: Prescription Medicine

Packs of 20 capsules: Pharmacy Only Medicine

8. SPONSOR

Pfizer New Zealand Ltd
P O Box 3998
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New Zealand.

Toll Free Number: 0800 736 363.
www.pfizermedicalinformation.co.nz

9. DATE OF FIRST APPROVAL

31 December 1969

10. DATE OF REVISION OF THE TEXT

13 November 2023

® Registered trademark.

Summary table of changes

Section changed	Summary of new information
Throughout	Minor editorial changes.
4.3	Revision of cross reference to section 6.1.
4.4, 4.8	Addition of adverse effect, generalised bullous fixed drug eruption (GBFDE).
6.5	Addition of statement regarding marketing of presentations.
8	Addition of sponsor's website address.