SCHEDULING STATUS S4

1. NAME OF THE MEDICINE
ANAMIDE 200 Tablet
ANAMIDE 300 Tablet capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each **ANAMIDE** 150 capsule contains 150 mg valproic
Each **ANAMIDE** 200 capsule contains 200 mg valproic

Contains sugar

ANAMIDE 150 contains 23.50 mg lactose monohydrate
ANAMIDE 200 contains 31.33 mg lactose monohydrate
For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM
ANAMIDE 200 mg capsules are opaque, white with blue bands on cap and body reverse printed white with "ANAMIDE 200" and "200" on the cap.
ANAMIDE 200 mg capsules are opaque, white with gold bands on cap and body reverse printed white with "ANAMIDE 300" and "300" on the cap.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Treatment of manic episodes of bipolar affective disorder in adolescents and in adults.
Treatment of bipolar disorder in children.
Treatment of limit to moderate post-operative pain.
Treatment of limit to moderate post-traumatic pain.
Treatment of limit to moderate primary dysmenorrhoea.
Prophylaxis of migraine and cluster headache.

4.2 Posology and method of administration
As the cardiovascular risks of ANAMIDE may increase with dose and duration of exposure, the lowest effective dose should be used. Treatment should be reviewed regularly and discontinued if appropriate.

Administration
The recommended daily dose is 200 mg, taken as a single dose or as two divided doses. Doses up to 1000 mg have been given in adults.

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

Post-acute phase
The recommended dose is 100 mg to 200 mg, up to a maximum daily dose of 400 mg. Dosing interval: 2 times per day (every 12 hours).

Acute phase
The recommended dose is 200 mg, up to a maximum daily dose of 600 mg. Dosing interval: 2 times per day (every 12 hours).

Dose is normally given orally.
Dose is normally given orally. Some patients may benefit from an additional 200 mg dose at bedtime.

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The recommended daily dose is 200 mg, taken as a single dose or as 100 mg twice daily. Some patients may benefit from an additional 200 mg dose at bedtime.

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Dosing adjustments
Hepatic impairment
Contraindicated in adolescents in patients with mitot hepatic impairment. Intrinsic **ANAMIDE** at risk of fatal hepatotoxicity in patients with severe hepatic impairment. There is no clinical experience in patients with severe hepatic impairment (See sections 4.3 and 5.2).

Renal impairment
Dose adjustment is not required in patients with mild to moderate renal impairment. There is no clinical experience in patients with severe renal impairment. (See sections 4.3 and 5.2).

Elderly
Elderly adjustment is not required.
Dose adjustment is not required in patients. Use with caution in elderly patients with a body mass of 50 kg or less is advisable to initiate therapy at the lowest recommended dose.

Paediatric
As to date are available, **ANAMIDE** is not recommended in persons under 18 years old.

Method of administration
Oral use. Take with food to minimize gastrointestinal upset. Swallow whole with a glass of water.

4.3 Contraindications
Hypersensitivity to valproic acid, or any other excipient of **ANAMIDE** (see section 6.1).
Severe hepatic impairment (person albumin < 25 g/l or Child-Pugh score > 10).
Severe renal impairment (creatinine clearance < 10 ml/min/1.73 m²).
Acute, chronic or alcoholic liver disease (characterized by jaundice or non-alcoholic anti inflammatory drugs (NSAIDs), including other cyclooxygenase-2 (COX-2) specific inhibitors.
Patients with a family history of severe hepatotoxicity associated with valproic acid.
Patients with hepatic porphyria (e.g. acute intermittent porphyria, variegate porphyria, porphyria cutanea tarda, porphyria cutanea tarda, porphyria cutanea tarda).
Acute pancreatitis or gastrointestinal GI bleeding.
Urea cycle disorders.
Pregnancy and women of childbearing potential not using contraceptive methods.
Breastfeeding women, unless the potential for human risk in pregnancy is unknown but cannot be excluded.
Concomitant mefloquine (see section 4.5).

4.4 Special warnings and precautions

ANAMIDE may increase the risk of cardiovascular incidents, cerebrovascular incidents, gastrointestinal events or unknown reactions that may be fatal.

Patients with a history of **ANAMIDE** have not been established for treatment excessive 12 weeks of cardiovascular and 24 weeks in rheumatoid arthritis.

Cardiovascular risk factors
Cardiovascular risk factors (e.g. diabetes, smoking, hypertension, hyperlipidemia, hyperuricemia, hyperhomocysteinemia, hypercoagulability, obesity, overweight, physical inactivity, family history of premature cardiovascular disease, cardiovascular disease, cerebrovascular disease, peripheral arterial disease, or thrombosis) should be assessed and managed in order to reduce the risk of cardiovascular events. Patients with a high cardiovascular risk profile should be carefully monitored and treatment with **ANAMIDE** should be considered only after careful consideration of the risk-benefit balance. Patients with a history of gastrointestinal disease, such as peptic ulceration, gastrointestinal bleeding, or inflammatory bowel disease, should be carefully monitored and treatment with **ANAMIDE** should be considered only after careful consideration of the risk-benefit balance. Patients with a history of gastrointestinal disease, such as peptic ulceration, gastrointestinal bleeding, or inflammatory bowel disease, should be carefully monitored and treatment with **ANAMIDE** should be considered only after careful consideration of the risk-benefit balance.

Intrinsic **ANAMIDE** is taken concomitantly with aspirin (even at low doses), there is further increase in the risk of gastrointestinal ulcers and bleeding. Patients taking concomitant aspirin should be carefully monitored and treatment with **ANAMIDE** should be considered only after careful consideration of the risk-benefit balance.

A significant difference in GI safety between selective COX-2 inhibitors plus aspirin vs NSAIDs plus aspirin has not been established in long-term clinical trials.

Concomitant NSAIDs
Be concomitant use of **ANAMIDE** and a non-aspirin NSAID should be avoided.

Cardiovascular effects
Cardiovascular effects are a concern for long-term treatment with **ANAMIDE** in **ANAMIDE**. Therefore, **ANAMIDE** should be used with caution in patients with history of cardiac failure, ischemic heart disease, peripheral arterial disease and cerebrovascular disease, or hypertension. Physicians should consult with cardiovascular specialists on assessment of these functions and risk factors.

Caution is also required in patients taking diuretic treatment or otherwise at risk of hypovolemia.

Caution also is required in patients with a history of congestive heart failure or hypertension.

Gastrointestinal
Serious GI adverse events (ulcers) 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. Hypertension should be closely monitored and treated with NSAIDs, including **ANAMIDE**, should be carefully considered, and blood pressure should be closely monitored during treatment with **ANAMIDE**.

Fluid retention
Fluid retention has been observed in some patients taking NSAIDs, including **ANAMIDE**. Therefore, **ANAMIDE** should be used with caution in patients with history of cardiac failure, ischemic heart disease, peripheral arterial disease and cerebrovascular disease, or hypertension. Physicians should consult with cardiovascular specialists on assessment of these functions and risk factors.

Caution also is required in patients taking diuretic treatment or otherwise at risk of hypovolemia.

Caution also is required in patients with a history of congestive heart failure or hypertension.

Hepatic
Serious adverse events (ulcers) 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. Hypertension should be closely monitored and treated with NSAIDs, including **ANAMIDE**, should be carefully considered, and blood pressure should be closely monitored during treatment with **ANAMIDE**.

Caution is also required in patients with hepatic porphyria, because it may trigger an attack in susceptible patients.

Caution should be used when initiating treatment in patients with dehydration. It is advisable to first correct dehydration in patients taking **ANAMIDE** treatment.

Caution is also required in patients with a history of congestive heart failure or hypertension