To whom it may concern:

Availability of Aspire Pharma's Products

Aspire Pharma fully understand that when undertaking a switch, availability of the products concerned is essential. If patients cannot get their medicines it can lead to loss of confidence or inconvenience to everyone concerned: Medicines Management teams, GPs, pharmacists and patients.

As part of Aspire Pharma's commitment to work in partnership with the NHS, to ensure that there are no stock issues experienced, we have ensured that all of the mainline wholesalers listed below carry stocks of Biquelle® XL (quetiapine), Gatalin® XL (galantamine), Neditol® XL (tolterodine), Repinex® XL (ropinirole), Sevodyne® (buprenorphine) and Vencarm® XL (venlafaxine) as standard. This means that pharmacies can obtain the products on a daily delivery.

- Alliance/Unichem
- AAH
- Phoenix
- Mawdsleys

We also hold large volumes of product at our warehouse at all times. If you have a requirement for a local wholesaler not listed above to supply Aspire Pharma's products, we will be happy to arrange this.

In addition to the normal level of stocks that the above wholesalers hold, if Aspire Pharma are made aware of an intention to switch to our products, as part of our service, we will contact all the local wholesalers and arrange for them to order in extra stocks to ensure that no issues are incurred by the patients.

Yours faithfully

Richard Condon
Chief Executive Officer

Aspire Pharma Limited
4 Rotherbrook Court Bedford Road Petersfield Hampshire GU32 3QG
T: +44 01730 231148 W: **www.aspirepharma.co.uk** E: info@aspirepharma.co.uk

Registered in England no. 6828501 Registered Address: 102 High Street Godalming Surrey GU7 1DS England

Biquelle XL (Quetiapine) Prolonged-release Tablets Prescribing Information (please refer to the full SmPC before prescribing)

Indications: Schizophrenia; moderate to severe manic and major depressive episodes in bipolar disorder; prevention of recurrence of manic or depressed episodes in bipolar patients who have previously responded to quetiapine treatment; add-on treatment of major depressive episodes in patients with major depressive disorder (MDD) who have had sub-optimal response to antidepressant monotherapy. **Available strengths:** 50, 150, 200, 300, 400mg (x60 tablets) and 600mg (x30 tablets). **Dosage**: Schizophrenia, moderate to severe manic episodes in bipolar disorder: Administer at least one hour before meal. 300mg day 1, 600mg day 2; recommended daily dose 600mg; max dose 800mg daily. Major depressive episodes in bipolar disorder: Administer at bedtime. 50mg day 1; 100mg day 2; 200mg day 3, 300mg day 4. Recommended daily dose 300mg; Doses over 300mg at experienced physician's discretion. Preventing recurrence in bipolar disorder: Continue on the same dose between 300-800mg at bedtime. For add-on treatment of major depressive episodes in MDD: Administer prior to bedtime. 50mg (day 1 & 2), 150mg (day 3 & 4), dose may be increased to 300mg/day on individual patient evaluation. Maintain at lowest effective dose. **Administration**: Once daily without food. Swallow tablets whole - do not split, chew, or crush. Patients on quetiapine immediate-release tablets may be switched to quetiapine prolonged-release tablets at equivalent total daily dosage taken once daily. Individual dose adjustments may be necessary. **Contraindications:** Patients with hypersensitivity to active substance or excipients; concomitant use of cytochrome P450 CYP 3A4 inhibitors (e.g., HIV protease inhibitors, azole-antifungal agents, erythromycin, clarithromycin, nefazodone). **Special warnings and precautions for use:** Elderly – use with caution. Rate of titration may need to be slower and daily dose lower. Start on 50mg/day and increase by 50mg/day to effective dose depending on response and tolerability. In elderly with major depressive episodes in MDD, start with 50mg/day on Days 1-3, 100mg/day on Day 4, 150mg/day on Day 8. Based on individual patient, if dose increase to 300mg/day required, this should not be before Day 22. Efficacy and safety not evaluated in bipolar patients over 65 with depressive episodes. Long-term efficacy and safety in MDD patients has been evaluated as monotherapy but not as add-on therapy. Not recommended for use in children and adolescents <18 years old due to lack of data. No dose adjustment necessary in renal impairment. Use with caution if known hepatic impairment – start on 50mg/day and increase by 50mg/day to effective dose, depending on response and tolerability. Closely supervise and monitor patients, especially those at high risk, for worsening, suicidal behaviour/thoughts and unusual changes in behaviour, particularly in early treatment and after dose changes -; assess metabolic parameters at initiation of and regularly throughout treatment; observe for signs and symptoms of hyperglycaemia; diabetic patients and those at risk for diabetes mellitus should be monitored regularly for worsening glucose control; consider dose reduction/ discontinuation if symptoms of tardive dyskinesia – symptoms can worsen or even arise after treatment discontinuation; discontinue if neuroleptic malignant syndrome develops and treat appropriately; if akathisia develops, increasing dose may be detrimental; if somnolence occurs, onset usually within first 3 days of treatment; orthostatic hypotension has been reported, usually during titration – can increase risk of falls, especially in elderly; caution in those with cardiovascular disease, risk factors for VTE, cerebrovascular disease, other conditions predisposing to hypotension, elderly patients with Parkinson's disease/parkinsonism, patients receiving concomitant CNS depressants and those at risk for sleep apnoea (e.g. overweight/male), history of seizures, risk factors for neutropenia, concomitant use of medications with anti-cholinergic (muscarinic) effects, diagnosis or history of urinary retention, prostatic hypertrophy, increased intraocular pressure/narrow angle glaucoma, family history of QT prolongation, risk factors for stroke, risk of aspiration pneumonia, history of alcohol or drug abuse. Caution when used with medicines known to cause electrolyte imbalance or increase QT interval, or with neuroleptics, especially in elderly, those with congenital long QT syndrome, congestive heart failure, heart hypertrophy, hypokalaemia, hypomagnesaemia, or in combination with other centrally acting medicines or alcohol. In patients with suspected cardiomyopathy or myocarditis discontinuation of quetiapine should be considered. Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) which can be life threatening or fatal have been reported very rarely with quetiapine treatment. SCARs commonly present as a combination of: extensive cutaneous rash or exfoliative dermatitis, fever, lymphadenopathy, and possible eosinophilia. If signs and symptoms suggestive of these severe skin reactions appear, withdraw quetiapine immediately and consider alternative treatment. Constipation and intestinal obstruction have been reported, including fatalities in those at higher risk for obstruction including those taking multiple medicines that decrease intestinal motility and may not report constipation symptoms. Pancreatitis has been reported. Severe neutropenia has been reported, mostly within months of initiation. Discontinue if neutrophil count $<1.0x10^9$/L – monitor neutrophil count and for signs of infection. Consider neutropenia if infection or fever, especially if no predisposing factor. Advise to immediately report signs/symptoms of agranulocytosis/infection, promptly check white blood cell and absolute neutrophil count. Contains lactose; do not use if rare hereditary problems of galactose intolerance, the lapp lactase deficiency or glucose-galactose malabsorption. Do not consume grapefruit juice. Advise not to drive/operate machinery until individual susceptibility to quetiapine affecting a patient's mental alertness is known. False positive results reported in enzyme immunoassays for methadone and tricyclic antidepressants. Recommend confirmation of questionable immunoassay screening results by an appropriate chromatographic technique. Concomitant use with strong hepatic enzyme inducer could affect efficacy. If receiving a hepatic enzyme inducer, only initiate quetiapine if benefits outweigh risks of removing enzyme inducer. Any change in inducer must be gradual and if required, should be replaced with a non-inducer (e.g. sodium valproate). Data in combination with divalproex or lithium in manic episodes limited Not approved for dementia-related psychosis. Advise gradual withdrawal over 1-2 weeks to avoid acute withdrawal symptoms. Only use in pregnancy if benefits justify potential risks. If exposed to antipsychotics in third trimester, monitor newborns carefully for adverse events; lactation – decide whether to discontinue breast-feeding or discontinue quetiapine. **Side effects:** For full list of side effects consult SmPC. 'Very Common', 'Common' and 'Serious' side effects included in this prescribing information. Very common (≥1/10): decreased haemoglobin, elevations in serum triglycerides, elevations in total cholesterol (predominantly LDL), decreases in HDL cholesterol, weight gain, dizziness, somnolence, headache, extrapyramidal symptoms, dry mouth and withdrawal (discontinuation) symptoms. Common (≥1/100 to <1/10): leucopenia, decreased neutrophil count, eosinophils increased, hyperprolactinemia, decreases in total T4, decreases in free T4, decreases in total T3, increases in TSH, increased appetite, increased blood glucose to hyperglycaemic levels, abnormal dreams and nightmares, suicidal ideation and suicidal behaviour, dysarthria, tachycardia, palpitations, blurred vision, orthostatic hypotension, dyspnoea, constipation, dyspepsia, vomiting, elevations in serum alanine aminotransferase, elevations in gamma-GT levels, mild asthenia, peripheral oedema, irritability, pyrexia. Serious uncommon/rare/very rare/not known frequency: neutropenia, thrombocytopenia, anaemia, hypersensitivity (including allergic skin reactions), hyponatraemia, Diabetes Mellitus, exacerbation of pre-existing diabetes, seizure, tardive dyskinesia, syncope, QT prolongation, elevations in serum aspartate aminotransferase, bradycardia, agranulocytosis, metabolic syndrome, venous thromboembolism, pancreatitis, intestinal obstruction/ileus, hepatitis, priapism, neuroleptic malignant syndrome, hypothermia, elevations in blood creatine phosphokinase, anaphylactic reaction, inappropriate antidiuretic hormone secretion, angioedema, Stevens-Johnson syndrome, cardiopathy, myocarditis, stroke, rhabdomyolysis, toxic epidermal necrolysis, erythema multiforme, Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), cutaneous vasculitis, drug withdrawal syndrome neonatal.. **MA number:** PL 35533/0051-55. **Cost:** £29.45 for 50mg, £49.45 for 150mg, £49.45 for 200mg, £74.45 for 300mg, £98.95 for 400mg (x60 pack), £70.73 for 600mg (x30 pack). **MAH:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire, GU32 3QG, UK. **Legal category:** POM. **Date last reviewed:** May 2021. **Version Number:** 1010269093 v 11.0.

Aspire Pharma Limited
4 Rotherbrook Court Bedford Road Petersfield Hampshire GU32 3QG
T: +44 01730 231148 W: **www.aspirepharma.co.uk** E: info@aspirepharma.co.uk

Registered in England no. 6828501 Registered Address: 102 High Street Godalming Surrey GU7 1DS England

GATALIN XL (Galantamine) Prolonged-release Capsules Prescribing Information (please refer to the full SmPC before prescribing)

Indications: Symptomatic treatment of mild to moderately severe dementia of the Alzheimer type in adults. **Available Strengths:** 8, 16 and 24mg x 28 capsules. **Dosage and method of use:** Diagnosis of probable Alzheimer type dementia should be confirmed before starting treatment according to current clinical guidelines. Therapy should occur under supervision of a physician, and with an available carer who will regularly monitor treatment intake. Administer once daily in morning preferably with food, and swallow whole with liquid. Do not crush or chew capsules. Ensure adequate fluid intake during treatment. Recommended starting dose: 8mg/day for 4 weeks. Initial maintenance dosing: 16mg/day for at least 4 weeks. Consider increase of maintenance dose to 24mg/day on individual basis after appropriate assessment. Consider dose reduction to 16mg/day if not showing increased response or not tolerating 24mg/day. Reassess tolerance and dosing regularly within first 3 months of treatment and thereafter. Consider discontinuing when evidence of therapeutic effect no longer present, or treatment not tolerated. No rebound effect after abrupt discontinuation. If switching from galantamine immediate-release to Gatalin XL, administer same total daily dose. If switching to once-daily regimen, take last dose of immediate-release tablets/oral solution in evening and start Gatalin XL once daily following morning. Consider dose reductions if treated with potent CYP2D6 or CYP3A4 inhibitors. If moderately impaired hepatic function (Child-Pugh score 7-9), start with 8mg once every other day, preferably taken in morning, for 1 week, thereafter proceed with usual starting dose. Daily dose should not exceed 16mg in these patients. **Contraindications:** Hypersensitivity to galantamine or any excipients; patients with both significant renal and hepatic dysfunction; creatinine clearance less than 9ml/min; severe hepatic impairment (Child-Pugh score greater than 9). **Special warnings and precautions for use**: Serious skin conditions e.g. Stevens-Johnson syndrome have been reported; inform patients about signs of serious skin reactions; discontinue at first appearance of skin rash. Monitor patient's weight. May have vagotonic effect on heart rate including bradycardia and atrioventricular node block – caution in 'sick sinus syndrome', supraventricular cardiac conduction disturbances, uncorrected electrolyte disturbance, medicines reducing heart rate e.g. digoxin, beta-blockers. Caution in patients with cardiovascular diseases e.g. immediate post-myocardial infarction, new-onset atrial fibrillation, second degree heart block or greater, unstable angina pectoris, congestive heart failure, and cerebrovascular diseases. Caution should be observed in patients with prolongation of the QTc interval, in patients treated with drugs affecting the QTc interval, or in patients with relevant pre-existing cardiac disease or electrolyte disturbances. Also caution in those at increased risk of developing peptic ulcers, history of severe asthma, obstructive pulmonary disease or active pulmonary infections. Not recommended if gastrointestinal obstruction or recovering from gastrointestinal surgery, in patients with urinary outflow obstruction or recovering from bladder surgery. Seizures have been reported. **Interactions:** Do not give concomitantly with other cholinomimetics e.g. ambenonium, donepezil, neostigmine, pyridostigmine, rivastigmine, systemic pilocarpine. Potential to antagonise effect of anticholinergics. If anticholinergics abruptly stopped, potential risk that galantamine effect exacerbated. Interaction possible with medicines that reduce heart rate e.g. digoxin, beta-blockers, calcium channel blockers, amiodarone. Caution with medicines that have potential to cause torsades de pointes - consider an ECG. May exaggerate succinylcholine-type muscle relaxation during anaesthesia, especially if pseudocholinesterase deficient. Consider galantamine dose reduction if treated with potent CYP2D6 or CYP3A4 inhibitors. **Pregnancy and breastfeeding:** Do not use while breast-feeding. Caution in pregnant women. **Ability to drive/use machines:** Minor/moderate influence on ability to drive and use machines – possible dizziness and somnolence. Not recommended in children. **Side effects:** For full list of side effects consult SmPC. 'Very Common' 'Common' and 'Serious' side effects included in the prescribing information. Very common (≥1/10): vomiting, nausea. Common (≥1/100 to <1/10): decreased appetite, hallucination, depression, syncope, dizziness, tremor, headache, somnolence, lethargy, bradycardia, hypertension, abdominal pain, abdominal pain upper, diarrhoea, dyspepsia, abdominal discomfort, muscle spasms, fatigue, asthenia, malaise, weight decreased, fall, laceration. Uncommon Serious (≥1/1000 to <1/100): hypersensitivity, seizures, supraventricular extrasystoles, atrioventricular block first degree, sinus bradycardia, palpitations, hepatic enzyme increased. Rare Serious (≥1/10000 to <1/1000): hepatitis, Stevens-Johnson Syndrome, acute generalized exanthematous pustulosis, erythema multiforme, atrioventricular block complete. **MA number:** PL 35533/0015-0017. **Cost:** £25.94 for 8mg; £32.45 for 16mg; £39.90 for 24mg (x28). **MAH:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire, GU32 3QG. **Legal category:** POM. **Date last reviewed:** April 2021. **Version number:** 10100671179 v 1.0

NEDITOL XL (Tolterodine) Prolonged-release Capsules Prescribing Information (please refer to the full SmPC before prescribing)

Indications: Symptomatic treatment of urge incontinence and/or increased urinary frequency and urgency as may occur in patients with overactive bladder syndrome. **Available strengths:** 2mg and 4mg x 28 prolonged-release capsules. **Dosage and method of use**: 4mg once daily except in patients with impaired liver or kidney function for whom recommended dose is 2mg once daily. In case of troublesome adverse reactions dose may be reduced from 4mg to 2mg once daily. Effect of treatment should be re-evaluated after 2-3 months. Take capsules with or without food and swallow whole. Not recommended for children. **Contraindications:** Hypersensitivity to the active substance or any excipient, urinary retention, uncontrolled narrow angle glaucoma, myasthenia gravis, severe ulcerative colitis, toxic megacolon. **Special warnings and precautions for use:** Use with caution in patients with significant bladder outlet obstruction at risk of urinary retention, gastrointestinal obstructive disorders, renal impairment, hepatic disease, autonomic neuropathy, hiatus hernia, at risk of decreased gastrointestinal motility, risk factors for QT prolongation including: congenital or documented acquired QT prolongation, electrolyte disturbances such as hypokalaemia, hypomagnesaemia and hypocalcaemia, bradycardia, relevant pre-existing cardiac diseases, concomitant administration of drugs known to prolong QT-interval including Class IA and Class III anti-arrhythmics. Avoid concomitant treatment with potent CYP3A4 inhibitors. Consider organic reasons for urge and frequency before treatment. Capsules contain lactose and sodium. Patients with rare hereditary problems of galactose intolerance, the total lactase deficiency or glucose-galactose malabsorption should not take this medicine. Concomitant treatment with other drugs possessing antimuscarinic properties may result in more pronounced therapeutic effect and side effects. Conversely, therapeutic effect of tolterodine may be reduced by concomitant administration of muscarinic cholinergic receptor agonist. Effect of prokinetics like metoclopramide and cisapride may be decreased by tolterodine. As may cause accommodation disturbances and influence reaction time, ability to drive/ use machines may be negatively affected. **Pregnancy/lactation:** Not recommended during pregnancy; avoid during lactation. **Side effects:** For the full list of side effects consult SmPC. 'Very Common' 'Common' and 'Serious' side effects included. Very common (≥1/10): dry mouth; Common (≥1/100 to <1/10): sinusitis, dizziness, somnolence, headache, dry eyes, abnormal vision (including abnormal accommodation), dyspepsia, constipation, abdominal pain, flatulence, diarrhoea, dysuria, fatigue, peripheral oedema. Serious Uncommon (≥1/1000 to <1/100): hypersensitivity, cardiac failure, arrhythmia, urinary retention. Serious (unknown frequency): anaphylactoid reactions, tachycardia, angioedema. Cases of aggravation of symptoms of dementia have been reported after tolterodine therapy was initiated in patients taking cholinesterase inhibitors for treatment of dementia. **MA number:** PL 35533/0148-0149 **Cost** £12.89 for 4mg x 28, £11.60 for 2mg x 28. **MAH:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire GU32 3QG. **Legal category:** POM. **Date last reviewed:** April 2021. **Version number:** 1010083024 v 6.0

Repinex XL (Ropinirole) Prolonged-Release Tablets (please refer to the full SmPC before prescribing)

Indications: Initial treatment in adults of Parkinson's disease as monotherapy to delay the introduction of levodopa or in combination with levodopa, over the course of the disease, when levodopa effect wears off or becomes inconsistent and fluctuations in therapeutic effect occur. **Available strengths:** Repinex XL (ropinirole) 2, 4, and 8mg x 28 tablets. **Dosage and method of use**: Tablets to be taken once daily, at similar time each day, with or without food, and swallowed whole. Starting dose is 2mg once daily for first week, then increased to 4mg once daily from the second week of treatment. If symptomatic control not achieved, daily dose may be increased by 2mg at weekly or longer intervals up to 8mg once daily; if symptomatic control still not achieved, daily dose may be increased by 2-4mg at 2 weekly or longer intervals. Maximum daily dose is 24mg. Patients should be maintained on the lowest dose that achieves symptomatic control. When given as adjunct to levodopa, may be able to gradually reduce levodopa dose, depending on response. In advanced Parkinson's Disease patients taking Repinex XL tablets in combination with levodopa, dyskinesias can occur during initial titration of Repinex XL tablets. In clinical trials, a reduction in levodopa dose was shown to potentially ameliorate dyskinesia. If treatment interrupted for one day or more, consider re-initiation by dose titration on ropinirole immediate-release tablets. Discontinue ropinirole treatment gradually over one week. In end stage renal disease where on haemodialysis, recommended initial dose 2mg once daily. Escalate dose according to tolerability and efficacy. Recommended maximum dose 18mg/day. Consider slower titration in patients aged 75 years or older. **Contraindications:** Hypersensitivity to active substance or excipients; severe renal impairment (creatinine clearance <30 ml/min) without regular haemodialysis; hepatic impairment. **Special warnings and precautions for use:** Inform patients that ropinirole is associated with somnolence and episodes of sudden sleep onset during daily activities, particularly in Parkinson's disease. Advise caution while driving or operating machines. If have experienced somnolence and/or an episode of sudden sleep onset, must refrain from driving or operating machines and consider dose reduction or termination. Due to risk of hypotension, blood pressure monitoring recommended, especially at start of treatment, in patients with severe cardiovascular disease (especially coronary insufficiency). If history of major psychotic disorders, only treat with dopamine agonists if benefits outweigh risks. Regularly monitor for development of impulse control disorders, including pathological gambling, increased libido, hypersexuality, compulsive spending/buying, binge or compulsive eating and if symptoms develop, consider dose reduction/tapered discontinuation. If rapid gastrointestinal transit, risk of incomplete release of active substance and residue being passed in the stool. Symptoms suggestive of neuroleptic malignant syndrome have been reported with abrupt withdrawal of dopaminergic therapy – therefore recommend tapering treatment. Dopamine agonist withdrawal syndrome: May occur when tapering or discontinuing dopamine agonists including ropinirole – possible higher risk with impulse control disorders and those on high daily dose and/or high cumulative doses. Symptoms include apathy, anxiety, depression, fatigue, sweating and pain and do not respond to levodopa – inform patients before tapering off and discontinuing ropinirole and closely monitor.

If severe and/or persistent symptoms, consider temporary re-administration of ropinirole at lowest effective dose. Inform patients that hallucinations can occur. Repinex XL 2mg contains lactose - not to be used in patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption. Repinex XL 4mg contains sunset yellow (E110) - may cause allergic reactions in patients with sunset yellow sensitivity. **Interactions:** Concomitant treatment with neuroleptics and other centrally active dopamine antagonists e.g. sulpiride or metoclopramide, should be avoided. Increased ropinirole plasma concentrations observed in patients treated with high doses of oestrogens - if hormone replacement therapy is stopped or introduced during treatment with ropinirole it may be necessary to adjust the ropinirole dose. Ropinirole principally metabolised by CYP1A2 - in patients on ropinirole, dose may need to be adjusted when medicines known to inhibit CYP1A2, e.g., ciprofloxacin, enoxacin, cimetidine or fluvoxamine, are introduced or withdrawn. Smoking induces CYP1A2 metabolism - if patients stop or start smoking during treatment with Repinex XL, dose adjustment may be required. **Pregnancy and lactation:** Repinex XL not recommended during pregnancy and should not be used during lactation. Not recommended for children below 18 years of age. **Ability to drive:** May have major effect on ability to drive/use machines. Refrain from driving/using machines if presenting with somnolence or sudden sleep episodes. **Side effects:** When Repinex XL is used as a monotherapy, side effects include: Very Common (≥1/10): somnolence, syncope, nausea; Common (≥1/100 to <1/10): dizziness (including vertigo), sudden onset of sleep, hallucinations, constipation, vomiting, heartburn, abdominal pain, peripheral oedema, leg oedema; Uncommon (≥1/1,000 to <1/100): excessive daytime somnolence, psychotic reactions (other than hallucinations) including delirium, delusion, paranoia, postural hypotension, hypotension; Not known (cannot be estimated from the available data): Impulse control disorders e.g. pathological gambling, increased libido, hypersexuality, compulsive shopping, binge eating, aggression, hypersensitivity reactions (including urticaria, angioedema, rash, pruritus), hepatic reactions, mainly increased liver enzymes, dopamine dysregulation syndrome, dopamine agonist withdrawal syndrome When Repinex XL is used as an adjunct therapy, side effects include: Very Common (>1/10): dyskinesia, somnolence, nausea; Common (≥1/100 to <1/10): dizziness (including vertigo), somnolence, sudden onset of sleep, hallucinations, confusion, postural hypotension, hypotension, heartburn, nausea, constipation, peripheral oedema; Uncommon (≥1/1,000 to <1/100): excessive daytime somnolence, psychotic reactions (other than hallucinations) including delirium, delusion, paranoia, postural hypotension, hypotension; Not known (cannot be estimated from the available data): Impulse control disorders e.g. pathological gambling, increased libido, hypersexuality, compulsive shopping, binge eating, hypersensitivity reactions (including urticaria, angioedema, rash, pruritus), hepatic reactions, mainly increased liver enzymes, dopamine agonist withdrawal syndrome. **MA number:** PL 35533/0023-0025. **Cost:** £6.20 for 2mg x 28 pack, £12.50 for 4mg x 28 pack, £21.00 for 8mg x 28 pack. **MAH:** Aspire Pharma Limited, Unit 4 Rotherbrook Court, Bedford Road, Petersfield, Hampshire, GU32 3QG, United Kingdom. **Legal Category:** POM. **Date last reviewed:** August 2020. **Version number:** 1010112063 V 9.0.

Sevodyne (buprenorphine) Transdermal Patches Prescribing Information (please refer to the full SmPC before prescribing)

Indications: For treatment of non-malignant pain of moderate intensity when opioid necessary for obtaining adequate analgesia, in adults. **Available Strengths:** Transdermal patches 5µg/hr, 10µg/hr, 15 µg/hr and 20µg/hr over a 7-day period, 4 patches per pack. **Dosage and method of use:** Prior to starting treatment with opioids, a strategy should be put in place with patients for ending treatment in order to minimise the risk of addiction and drug withdrawal syndrome**.** Administer every 7th day. Use lowest dose (5µg/hr) as initial dose with consideration given to opioid history and medical status of patient. During initiation of treatment, short-acting supplemental analgesics may be required. During titration process, dose may be adjusted every 3-days (72 hours). Thereafter, 7-day dosing interval should be maintained. Subsequent dose increases may be titrated based on need for supplemental pain relief and patient's analgesic response to patch. To increase dose, replace with larger patch or combination of patches applied in different places to achieve desired dose. Recommended that no more than 2 patches be applied at same time, to maximum total dose of 40µg/hr. Do not apply new patch to same skin site within 3-4 weeks. Monitor regularly to assess optimum dose and duration of treatment. Possibility of hyperalgesia, tolerance, and progression of underlying disease should be considered if inadequate pain control. Consider Sevodyne dose reduction, discontinuation or treatment review.. If long-term pain treatment necessary, careful and regular monitoring required. Buprenorphine concentrations decrease gradually after patch removal. Subsequent opioid should not be administered within 24 hours after patch removal. Sevodyne can be used as an alternative to other opioids. No dose adjustment necessary in renal impairment or the elderly. Monitor patients with hepatic insufficiency; if severe hepatic impairment, consider alternate therapy. Apply to non-irritated, intact skin of upper outer arm, upper chest, upper back or side of chest. Patch must not be divided or cut in, to pieces. **Contraindications:** In patients: with known hypersensitivity to buprenorphine or excipients; who are opioid dependent and for narcotic withdrawal treatment; have conditions in which respiratory centre and function are severely impaired or may become so; receiving MAO inhibitors or have taken them within the last two weeks; suffering from myasthenia gravis or delirium tremens. **Special warnings and precautions for use**: Caution in patients with respiratory depression, CNS depressants co-administration, serotonergic agents, psychological dependence, abuse profile and history of substance abuse, acute alcohol intoxication, sleep apnoea, head injury, shock, reduced level of consciousness of uncertain origin, intracranial lesions or increased intracranial pressure, severe hepatic impairment, constipation Significant respiratory depression associated with buprenorphine, particularly by intravenous route. Overdose deaths have occurred when addicts intravenously abused buprenorphine, usually with concomitant benzodiazepines. Caution when prescribing Sevodyne to patietns with or suspected drug or alcohol abuse or serious mental illness. In those physically dependent on full µ-opioid agonists, buprenorphine may precipitate an abstinence syndrome. Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. In patients who present with CSA, consider decreasing the total opioid dosage. Increased absorption of buprenorphine may occur if patches exposed to external heat sources. Fever in febrile patients may result in increased absorption and thereby increased risk of opioid reactions. Concomitant use of buprenorphine and other serotonergic agents may result in the potentially fatal serotonin syndrome - symptoms include mental-status changes, autonomic instability, neuromuscular abnormalities and/or gastrointestinal symptoms. Carefully monitor patients on concomitant serotonergic agents, especially during treatment initiation and dose increases. If serotonin syndrome suspected, consider dose reduction or discontinuation of therapy depending on symptom severity. For all patients, prolonged use may lead to drug dependence (addiction), even at therapeutic doses. Incomplete tolerance developed for some side effects e.g. opioid induced constipation. Risks increased if current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder. Consider additional support and monitoring if at risk of opioid misuse. Explain risks of developing tolerance. Overuse or misuse may result in overdose and/or death. Closely monitor for signs of misuse, abuse or addiction. Regularly review clinical need for analgesia. Sevodyne may cause positive reaction to sports doping control tests. Drug withdrawal syndrome may occur upon abrupt cessation. If withdrawal occurs, is generally mild, begins after 2 days, may last up to 2 weeks. Gradually taper the dose to minimise symptoms of withdrawal when therapy is no longer required. Tapering of a high dose may take weeks to months. Opioid withdrawal can manifest as: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other possible symptoms include irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate. Consider hyperalgesia if the patient on long-term opioid therapy presents with increased pain – may resolve with opioid dose reduction. Application site reaction usually mild or moderate skin inflammation (irritant contact dermatitis) – may include erythema, oedema, pruritus, rash, vesicles, burning sensation. Monitor application sites for reaction. Diagnostic procedure should be performed if allergic contact dermatitis suspected to determine if sensitisation has occurred and its cause. In patients taking CYP3A4 inhibitors, titrate dose carefully as reduced dosage might be sufficient. Not recommended for analgesia in immediate post-operative period or in situations characterised by narrow therapeutic index or rapidly varying analgesic requirement. Opioids may cause an increase in serum prolactin and decreases in plasma cortisol and testosterone with possible clinical symptoms. Use cautiously with other central nervous system depressants, benzodiazepines and serotonergic medicinal products due to increased risk of serotonin syndrome. The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effects. Only concomitantly prescribe sedative medicines if no other treatment options possible. The dose and duration of concomitant use should be limited. Inform patients of signs and symptoms of respiratory depression and sedation and monitor closely. **Pregnancy and Breastfeeding**: Not recommended during breastfeeding. Do not use during pregnancy or in women of childbearing potential not using effective contraception unless benefit justifies potential risk to foetus. If prolonged opioid use required in pregnancy, advise of risk of neonatal opioid withdrawal syndrome – ensure treatment available. Use during labour may depress neonate respiration – ensure antidote for child available**. Driving**: Patients should be warned about effect on driving and, if experiencing dizziness, drowsiness or blurred vision, they should not drive or use machines for at least 24 hours after patch removed **Side effects:** For the full list of side effects consult SmPC. 'Very Common' 'Common' and 'Serious' side effects are included in prescribing information. Very common (≥1/10) side effects: headache, dizziness, somnolence, constipation, nausea, vomiting, pruritus, erythema, application site reaction. Common (≥1/100 to <1/10) side effects: anorexia, confusion, depression, insomnia, nervousness, anxiety, tremor, dyspnoea, abdominal pain, diarrhoea, dyspepsia, dry mouth, rash, sweating, exanthema, muscular weakness, arthralgia, tiredness, asthenic conditions, peripheral oedema. Uncommon Serious (≥1/1000 to <1/100) side effects: hypersensitivity, tachycardia, circulatory collapse, drug withdrawal syndrome. Rare/very rare Serious (<1/10000 to <1/1000) side effects: anaphylactic reaction, psychotic disorder, angina pectoris, respiratory depression, respiratory failure, drug dependence. Unknown frequency Serious side effects: anaphylactoid reaction, seizures, neonatal drug withdrawal syndrome. **MA number:** PL 35533/0059-0061 (5µg/hr,10µg/hr, 20µg/hr). PL 35533/0135 (15 µg/hr). **Cost:** £5.53 for 5µg/hr patch x4 pack; £9.93 for 10µg/hr patch x4 pack; £15.48 for 15 µg/hr patch x4 pack and £18.09 for 20µg/hr patch x4 pack. **MAH:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire GU32 3QG. **Legal category:** POM. **Date last reviewed:** March 2022. **Version number:** 1010311145 v 13.0.

Vencarm XL (venlafaxine) Prolonged-release Capsules Prescribing Information (please refer to the full SmPC before prescribing)

Indications: Major depressive episodes (MDEs), prevention of recurrence of MDEs, generalised anxiety disorder (GAD), social anxiety disorder (SAD) and panic disorder, with or without agoraphobia. **Available strengths:** 37.5, 75, 150 and 225mg x 28 capsules. **Dosage**: MDEs: recommended starting dose 75mg once daily, if not responding, increase up to maximum 375 mg/day. GAD and SAD: recommended starting dose 75mg once daily. Panic disorder: 37.5mg/day for 7 days, then increased to 75mg/day. GAD, SAD and panic disorder patients not responding to 75mg/day increase up to maximum 225mg/day. For all indications maintain lowest effective dose; dose increases can be made at 2 weeks intervals or more; due to risk of dose-related adverse effects, only make dose increments after clinical evaluation; patients should usually be treated for several months or longer with regular reassessment. Caution in elderly. Not recommended in those under 18 years. Caution if GFR 30-70ml/min. In mild or moderate hepatic impairment, severe renal impairment (GFR < 30 ml/min) or haemodialysis reduce dose by 50%. Caution in severe hepatic impairment - reduce dose by more than 50%. Abrupt discontinuation should be avoided. Gradually reduce over several weeks/months to reduce risk of withdrawal reactions and monitor closely. Suicide/suicidal thoughts and aggression have been observed during venlafaxine dosing changes including discontinuation. Most commonly reported withdrawal symptoms: dizziness, sensory disturbances, agitation, nausea, vomiting, tremor, vertigo, headache, flu syndrome, visual impairment, hypertension. **Administration**: Take with food, at approximately same time each day. Swallow whole with fluid - do not divide, crush, chew, or dissolve. Patients on venlafaxine immediate-release tablets may be switched to venlafaxine prolonged-release capsules at nearest equivalent daily dosage. **Contraindications:** Hypersensitivity to active substance or excipients. Concomitant treatment with irreversible monoamine oxidase inhibitors (MAOIs) due to risk of serotonin syndrome. Do not initiate for at least 14 days after discontinuation of an irreversible/reversible MAOI. Discontinue for at least 7 days before starting an irreversible/reversible MAOI. **Special warnings/precautions for use:** Monitor patients for risk of suicide-related events until improvement occurs. Monitor for clinical worsening, suicidal behaviour or changes in behaviour. Observe carefully (risk of potentially life-threatening serotonin syndrome) if given concomitantly with other serotonergic agents e.g. SSRIs, SNRIs, triptans, amphetamines, lithium, sibutramine, St John's Wort, fentanyl and analogues, tramadol, buprenorphine, dextromethorphan, tapentadol, pethidine, methadone, pentazocine; agents that impair serotonin metabolism e.g. MAO-inhibitors, serotonin precursors e.g. tryptophan; or with antipsychotics and other dopamine antagonists, particularly during treatment initiation and dose increases. Reduce dose or discontinue if serotonin syndrome suspected. Monitor patients with raised intraocular pressure or at risk for acute narrow-angle glaucoma. Screen for high blood pressure and control pre-existing hypertension before starting treatment. Review blood pressure after starting treatment and dose increases. Caution in patients whose underlying conditions might be compromised by increases in blood pressure or heart rate, patients with recent history of myocardial infarction, unstable heart disease or at high risk of serious cardiac arrhythmia or QTc prolongation (consider risk-benefit balance). Caution if history or family history of bipolar disorder or aggression; if predisposition to bleeding, including use of anticoagulants or platelet inhibitors; if on diuretics or volume-depleted (risk of hyponatraemia/SIADH); use with caution if history of convulsions and discontinue in patients who develop seizures. Measure serum cholesterol during long-term treatment. Co-administration with weight loss agents not recommended. In patients who develop akathisia, increasing dose may be detrimental. Advise patients about importance of dental hygiene. In diabetic patients, insulin and/or oral antidiabetic dosage may need adjustment. SSRIs and SNRIs may cause symptoms of sexual dysfunction which may continue after discontinuation. SSRIs/SNRIs may increase the risk of postpartum haemorrhage. **Interactions:** Must not be used with irreversible, non-selective MAOIs; concomitant treatment with reversible, selective MAOIs and linezolid not recommended. Serotonin syndrome – if concomitant treatment with SSRI, SNRI or serotonin receptor agonist (triptan) clinically warranted, carefully observe, particularly when starting treatment and dose increases. Caution when used in combination with other CNS-active substances (advise patients to avoid alcohol), CYP3A4 inhibitors, lithium, imipramine, haloperidol, metoprolol. 150mg contains Allura red (E129) and Sunset Yellow FCF (E110) and 225mg contains Carmoisine (E122), which may cause allergic reactions. Avoid co-administration with medicines prolonging QTc interval (risk of QTc prolongation/ventricular arrhythmias). **Pregnancy/breastfeeding**: Only use in pregnancy if benefits outweigh risk. Discontinuation symptoms may be seen in newborns if used before birth. Potential increased risk of persistent pulmonary hypertension in newborn. Potential increased risk of postpartum haemorrhage if SSRI/SNRI exposure within month prior to birth. Risk to suckling child cannot be excluded – make decision to continue/discontinue breast-feeding or continue/discontinue Vencarm XL. **Effect on driving:** Caution patients on their ability to drive or operate hazardous machinery. **Side effects:** For full list of side effects consult SmPC. 'Very Common' 'Common' and 'Serious' side effects included in this prescribing information. Very common (≥1/10) side effects: insomnia, headache, dizziness, sedation, nausea, dry mouth, constipation and hyperhidrosis (including night sweats). Common (≥1/100 to <1/10) side effects: decreased appetite, confusional state, depersonalisation, abnormal dreams, nervousness, libido decreased, agitation, anorgasmia, akathisia, tremor, paraesthesia, dysgeusia, visual impairment, accommodation disorder, including vision blurred, mydriasis, tinnitus, tachycardia, palpitations, hypertension, hot flush, dyspnoea, yawning, diarrhoea, vomiting, rash, pruritus, hypertonia, urinary hesitation, urinary retention, pollakiuria, menorrhagia, metrorrhagia, erectile dysfunction, ejaculation disorder, fatigue, asthenia, chills, weight decreased, weight increased, blood cholesterol increased. Uncommon (≥1/1,000 to <1/100) serious side effects: gastrointestinal haemorrhage, LFT abnormal, angioedema. Rare serious (≥1/10,000 to <1/1,000) side effects: agranulocytosis, aplastic anaemia, pancytopenia, neutropenia, anaphylactic reaction, SIADH, hyponatraemia, neuroleptic malignant syndrome (NMS), serotonin syndrome, convulsion, angle-closure glaucoma, Torsades de Pointes, ventricular tachycardia, ventricular fibrillation, ECG QT prolonged, interstitial lung disease, pancreatitis, hepatitis, Stevens-Johnson syndrome, toxic epidermal necrolysis, erythema multiforme, rhabdomyolysis. Very rare (<1/10,000) serious side effects: thrombocytopaenia, tardive dyskinesia, mucosal haemorrhage, prolonged bleeding time. Not known (frequency cannot be estimated) serious side effects: suicidal ideation and behaviours, Stress cardiomyopathy (Takotsubo cardiomyopathy), postpartum haemorrhage. **MA number:** PL 35533/0074-0077 **Cost:** £3.30 for 37.5mg; £2.59 for 75mg; £3.89 for 150mg and £9.90 for 225mg (x28). **MAH:** Aspire Pharma Ltd, Unit 4, Rotherbrook Court, Bedford Road, Petersfield, Hampshire, GU32 3QG. **Legal category:** POM. **Date reviewed:** April 2022. **Version number:** 1010344190 v 6.0

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Aspire Pharma Ltd on 01730 231148.