Care issues with the appropriateness of the medicine/s?	**Licensed indications:** Substitution treatment for opioid drug dependence, within a framework of medical, social and psychological treatment.	
Care issue with the formulation of the medicine/s?	Buprenorphine sublingual tablets: 400micrograms, 2mg and 8mg Suboxone® (Buprenorphine/naloxone) sublingual tablets: 2mg/500mcg and 8mg/2mg	
Care issue with the dosage and frequency of the medicine/s?	Buprenorphine is a long acting opioid and the sublingual route is the only effective and safe route of administration. The tablet should be kept under the tongue until dissolved, which usually occurs within 5 minutes. Most regimes involve starting with a low dose and rapidly increasing. In Forth Valley the usual starting dose is 4mg followed by a further 4mg a few hours later on the first day in the clinic setting. A dose of 16mg is given on day two with further increase after a week if required. The majority of patients will be maintained on 12-16 mg/day however doses may be prescribed up to 32mg/day for buprenorphine and 24mg/day for suboxone®. Alternate day dosing may suit some patients.	
Care issue in relation to contraindications?	**Contraindications:** • Hypersensitivity to buprenorphine or to any of the excipients. • Severe respiratory insufficiency • Severe hepatic insufficiency • Acute alcoholism or *delirium tremens* • Breast feeding Due to the lack of data in adolescents (16-18), buprenorphine should be used only with caution in this age group. Patients should be closely monitored during the switching period from methadone to buprenorphine since withdrawal symptoms have been reported.	
Drug interaction with one or more medicines?	**Drug**	**Comment**
Is the patient prescribed other medicines which may interact? □ Yes □ No	Alcohol	Increased sedative effects
	Potent CYP3A4 inhibitors (e.g. azole antifungals such as ketoconazole or itraconazole, erythromycin, gestodene, troleandomycin, HIV protease inhibitors like ritonavir, indinavir, nelfinavir and saquinavir)	↑plasma concentrations Avoid combination or monitor closely, dose reduction may be required.
	CYP3A4 inducers has not been investigated but theoretical interaction e.g. phenobarbital, carbamazepine, phenytoin and rifampicine	May ↑ metabolism of buprenorphine Monitor closely
	Benzodiazepines:	Combination may result in death due to respiratory depression. Therefore, dosages must be individually titrated and the patient monitored carefully.
	CNS depressants: other opioid derivatives (analgesics and antitussives (e.g. methadone, dextropropoxyphene, codeine, dextromethorphan), certain antidepressants, sedative H_1-receptor antagonists, barbiturates, anxiolytics, neuroleptics, clonidine and related substances.	Combinations increase central nervous system depression and may also affect the ability to drive and operate machines.
	Monoamine oxidase inhibitors (MAOI):	Possible exaggeration of the effects of opioids

Side effects with one or more medicines? **Is the patient aware of common side effects of buprenorphine?** □ Yes □ No **Is the patient aware of the risks of toxicity and overdose?** □ Yes □ No **Is the patient aware of the signs and symptoms of overdose?** □ Yes □ No	The onset of side effects depends on the patient's tolerance threshold. Which is higher in drug addicts than in general population The symptoms most frequently observed are: - Constipation - Headaches - Insomnia - Asthenia - Drowsiness - Nausea and vomiting - Fainting and dizziness - Orthostatic hypotension - Sweating **Actions:** • **Check patient's understanding of the side effects of buprenorphine.** • **If side effects are experienced during initiation, provide reassurance that it may be transient. If it persists report to keyworker/prescriber.** • **If constipation is a problem, advise on fluid intake & dietary fruit/ fibre.** • **For a patient with more severe side effects contact their keyworker/ prescriber.** • **Record any care issues in the patient's care plan** The use of other substances in combination with buprenorphine increases the risk of toxicity and overdose. The use of buprenorphine with alcohol and/or benzodiazepines and/or heroin can be fatal! Signs and symptoms of opioid overdose include: • *Pinpoint pupils* • *Unrousable* • *Pale skin and blue lips* • *Shallow breathing/slow breathing* • *Snoring breaths/rasping breaths* **Actions:** • **Check if the patient has received overdose prevention training and is aware of the naloxone programme. If not then give naloxone leaflet and refer to Signpost Recovery.** • **Check if the patient understands the risks of using alcohol or other illicit substances with buprenorphine.** • **Check the patient's understanding of the signs of opiate overdose using the naloxone leaflet.** • **If the patient is showing signs of toxicity or intoxication withhold the buprenorphine. Where appropriate ask the patient to return after 3 or 4 hours and reassess. It may be more appropriate to ask the patient to return first thing the following morning for reassessment. Contact the keyworker/prescriber regarding the incident.** • **Immediately refer a patient suffering from signs of significant toxicity to their keyworker/prescriber, contacting their keyworker/prescriber to alert them.** • **When the patient reports adverse drug reactions, record using the MHRA Yellow Card Reporting Scheme.** • **Record any care issues in the patient's care plan and agree desired outcomes and actions.**
Problems with concordance? **Is the patient aware of the risks of precipitated withdrawal when commencing treatment?** □ Yes □ No **Is the patient taking their buprenorphine as prescribed?** □ Yes □ No	Buprenorphine is a long acting opioid which is used in the management of opioid dependence. Most regimes involve starting with a low dose and rapidly increasing. In Forth Valley the usual starting dose is 4mg followed by a further 4mg a few hours later on the first day in the clinic setting. A dose of 16mg is given on day two with further increase after a week if required. *The risk factors for overdose during induction are:* • *Low opioid tolerance* • *Use of CNS depressant drugs including alcohol* *There is also a risk of precipitating withdrawal, which is increased if insufficient time is left before administering buprenorphine in patients who have:* • *Recently used heroin, particularly at higher doses* • *Recently consumed long-acting opioids such as methadone* Risks can be minimised by careful assessment, frequent monitoring, supervised consumption and educating patients and carers of the early signs of overdose.

Does the patient know what to do if they miss a dose? □ Yes □ No	After three days without their regular prescribed buprenorphine dose, patients may have lost their tolerance and may be at risk of overdose if the usual dose is taken. • If a patient on daily pick up misses one dose then presents at the pharmacy on the following day the usual daily dose may be given. • If two doses are missed then the following day the daily dose may be supplied but report to the key worker/prescriber. • If three doses are missed then the following day withhold the dose and contact the prescriber for advice. • A missed daily dose should **never** be supplied. • Where a patient regularly misses occasional doses the keyworker/prescriber should be notified as this may indicate *the patient is not stable on their current treatment plan.* **Actions:** • **Check the patient's understanding of how and when to take their buprenorphine using the buprenorphine leaflet as a prompt for counselling the patient:** o **Advise the patient to take their buprenorphine at the same time each day.** o **Discuss when would be most convenient for the patient and the pharmacy. (Service should be available during all opening hours.)** o **For new patients complete the treatment agreement.** o **Advise the patient on what to do if they miss a dose.** o **Advise the patient on the safe storage of buprenorphine** • **Record any care issues in the patient's care plan and agree desired outcomes and actions.**
Care issue in relation to polypharmacy?	Evident from PMR
Pharmacokinetic risk factors?	Buprenorphine undergoes extensive first-pass hepatic metabolism therefore the oral route is inappropriate. Peak plasma concentrations are achieved 90 minutes after sublingual administration but most patients experience the effects at around 2-4 hours. Its clinical effects peak at 1-4 hours post dose Buprenorphine has a long half life. At therapeutic doses it can exert its effects for up to 48-72 hours. Buprenorphine is metabolised via cytochrome P450 CYP3A4.
Pharmacodynamic risk factors?	Buprenorphine is an opioid partial agonist/antagonist which attaches itself to the μ (mu) k (kappa) receptors of the brain. Its activity in opioid maintenance treatment is attributed to its slowly reversible link with the μ receptors which, over a prolonged period, minimises the need of the addicted patient for drugs. Buprenorphine has a high affinity for these receptors and has the capacity to precipitate rapid withdrawal if taken in the presence of other opioids.
Disease risk factor?	Opioid dependence
Taking one or more medicines with a narrow therapeutic range?	Buprenorphine does not have a narrow therapeutic range
Taking one or more black triangle medicines?	Buprenorphine is not a black triangle medicine
Duplication of medication	Evident from PMR
Summary: **Are there any pharmaceutical care issues of note?**	Summarise any issues which are apparent from answers to the questions above. This will aid the preparation of a pharmaceutical care plan if required.