

NHS lothian

Community Pharmacy Supply of Medicines for Hepatitis C

Pharmaceutical Care Information Pack

Introduction to Hepatitis C Infection

Chronic hepatitis C constitutes a major global health concern as it is a leading cause of chronic liver disease, cirrhosis and hepatocellular carcinoma. The goal of therapy is to prevent these complications through viral eradication.

The hepatitis C virus (HCV) was first identified in 1989 and HCV infection has become a major health problem worldwide. Approximately 0.8% of the Scottish population is thought to be chronically infected with HCV (around 37,500 individuals). The prevalence of infection varies between population groups ranging from 50% in people who inject drugs (PWID) to less than 0.04% among new blood donors.

Up to 80% of patients infected with HCV become chronically infected and most of these patients will show evidence of chronic hepatitis.

Hepatitis C is usually slowly progressive over a period of many years. Five to fifteen per cent of patients with chronic hepatitis may progress to liver cirrhosis over 20 years. Four to nine per cent of patients with cirrhosis will develop liver failure; and two to five per cent of patients with cirrhosis will develop primary hepatocellular carcinoma.

In the UK the two major routes of transmission of HCV have been sharing of drug injecting equipment by PWID and transfusion of infected blood or blood products. Virus inactivation treatment of blood products began in 1987 and since 1991, blood donations have been screened for hepatitis C, eliminating blood products as a source of HCV infection.

### **Genotypes**

HCV is characterised by genotypes and subgroups with prevalence varying depending on the geographical location. Genotype 1 can be further classified into subgroup a and b. Genotype 1 and 3 are the most prevalent in Scotland.

Genotype details are as follows:

* Genotype 1 occurs in around 50% of patients in Lothian
* Genotypes 2 occurs in less than 5% of patients; Genotypes 3 occur in around 45% of patients in Lothian; these subtypes are most prevalent in India, Pakistan, Thailand, Australia, and Scotland (PWID population)
* Genotype 4-6 occurs in less than 5% of patients; genotype 4 is most prevalent in the Middle East and Africa

Within a region, a specific genotype may also be associated with a specific mode of transmission, such as genotype 3 among persons in Scotland who abuse intravenous drugs.

Treatment of chronic HCV infection has 2 goals. The first is to achieve sustained viral eradication of HCV (i.e. sustained virologic response [SVR]), which is defined as the persistent absence of HCV RNA in serum 3 months or more after completing antiviral treatment. This represents cure of the infection. The second goal is to prevent progression to cirrhosis, hepatocellular carcinoma (HCC), and decompensated liver disease requiring liver transplantation.

Antiviral therapy for chronic hepatitis C should be determined on a case-by-case basis. However, treatment is generally recommended who meet the following criteria;

* Age greater than 18 years
* Positive HCV antibody and serum HCV RNA test results
* Willingness to be treated and to adhere to treatment requirements
* No contraindications for treatment

The treatment of hepatitis C has evolved over the years Historically, treatment for all genotypes consisted of combination therapy of ribavirin and pegylated interferon (PEG-IFN) for up to 48 weeks. The SVR (cure) rate with this combination was only around 60%. It had many unpleasant side-effects and some people may still think that this is the treatment being used now. In 2011, patients with genotype 1 had option of triple therapy in which a protease inhibitors, boceprevir or telaprevir were used in combination with ribavirin and peg-interferon which improved SVR rates. Since 2014, several new Direct Acting Antiviral (DAA) medicines have been licensed. These act directly on various parts of the viral replication life cycle, inhibiting specific proteins. **These treatments have a shorter treatment duration, minimal side effects and are expected to achieve SVR (cure) rates over 90%.** There are four classes of DAAs which are classed according to the protein they have action on, namely, NS3/4 protease inhibitors, NS5B nucleoside polymerase inhibitors, NS5B non nucleoside polymerase inhibitors and NS5A inhibitors.

Successful treatment of hepatitis C infection has been shown to reduce the risk of developing cirrhosis and for those with established cirrhosis, reduce the risk of decompensation and HCC. Importantly data from Scotland shows a reduction not just in liver related morbidity/mortality, but also all cause mortality, Data from Scotland and elsewhere demonstrate that successful treatment is also associated with a reduction in cardiovascular mortality, development of diabetes, and a lower risk of haematological malignancies.

The Scottish Government sets minimum treatment targets for health boards to achieve through the Scottish Blood Borne Virus Framework, and has signed up to the Glasgow Declaration – a WHO sponsored commitment to eliminate Hepatitis C as a public health concern by 2030.

# **Current HCV Medications**

The primary goal of HCV therapy is to cure the infection and prevent transmission, which leads to a reduction of patients developing the complications of the virus including cirrhosis and hepatocellular cancer (HCC)

In patients who achieve a SVR, antiviral agents shorten the clinical course of HCV, prevent complications, prevent subsequent recurrences and decrease transmission.

The following information provides a brief overview of the available treatment regimens. Further information can be found in the Summary of Product Characteristics ([www.medicines.org.uk](http://www.medicines.org.uk)). Drug-Drug Interaction information can also be found in the SPC as well as <https://www.hep-druginteractions.org>. The specialist team should be contacted if further information is required.

**Directly Acting Antiretrovirals (DAAs)**

**Ledipasvir/Sofosbuvir (Harvoni®)**

Ledipasvir/Sofosbuvir (Harvoni®) is a fixed dose combination tablet containing ledipasvir 90mg and sofosbuvir 400mg. Ledipasivir is a potent NS5A HCV inhibitor and sofosbuvir is a potent NS5B polymerase inhibitor. It is used in combination with sofosbuvir for treatment of genotype 1 and 4.

# Prescribing Information

Ledipasvir/sofosbuvir (harvoni®)­® is indicated for treatment of chronic hepatitis C infection mono-infection and HCV/HIV-1 co-infection. The treatment regimen and duration are dependent on both viral genotype and patient population. The current license recommends treatment courses up to 24 weeks. However, subsequent trial information has shown comparable results with course length shortened to 12 weeks, even if patient has been shown to be cirrhotic and/or treatment experienced. Therefore, in the vast majority of cases, treatment will be given for 12 weeks.

* Genotype 1 or 4

1 tablet (90mg/400mg) PO daily for 12 weeks

* + In patients who are treatment naïve and non-cirrhotic, treatment can be shortened to 8 weeks
	+ Ribavirin may be added depending on clinical circumstances;
	+ For paediatric dosing and formulations, see summary of product characteristics.

Ledipasvir/sofosbuvir (Harvoni®) can be used in all stages of liver disease (ie non-cirrhotic to decompensated cirrhosis)

### **Administration**

The film-coated tablet is for oral use. Patients should be instructed to swallow the tablet whole. The film-coated tablet should not be chewed or crushed, due to the bitter taste of the active substance. The tablet should be taken with or without food.

**Missed doses**

Patients should be instructed that if vomiting occurs within 5 hours of dosing, an additional tablet should be taken. If vomiting occurs more than 5 hours after dosing, no further dose is needed.

If a dose is missed and it is within 18 hours of the normal time, patients should be instructed to take the tablet as soon as possible and then patients should take the next dose at the usual time. If it is after 18 hours then patients should be instructed to wait and take the next dose at the usual time. Patients should not be instructed to take a double dose.

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**Pregnancy +/-concomitant use with ribavirin**

There is limited data on use of ledipasvir/sofosbuvir (Harvoni®) in pregnancy. As a precautionary measure, the manufacturer does not recommend use in pregnancy

When ledipasvir/sofosbuvir (Harvoni®) is used in combination with ribavirin, women of childbearing potential or their male partners must use two effective forms of contraception during the treatment and for a period of time after the treatment as recommended in the Summary of Product Characteristics for ribavirin.

**Effects on ability to drive and use machines**

Ledipasvir/sofosbuvir (Harvoni®) has a negligible influence on the ability to drive and use machines. Patients should be informed that fatigue was more common in patients treated with ledipasvir-sofosbuvir (harvoni®) than with placebo.

**Summary of safety profile**

Clinical trial data has shown that ledipasvir/sofosbuvir (Harvoni®) is well tolerated with the most common side effects reported are fatigue and headache. Further information about adverse effects can be found in the SPC.

**Drug-Drug Interactions**

Consult the summary of product characteristics ([www.medicines.org.uk](http://www.medicines.org.uk)) or [www.hep-druginteractions.org](http://www.hep-druginteractions.org) for safety of concomitant meds or discuss with specialist clinical pharmacist.

The interaction profile for ledipasvir/sofosbuvir (Harvoni®) is similar to that of sofosbuvir and any interactions identified for sofosbuvir may occur with ledipasvir/sofosbuvir (Harvoni®).

Ledipasvir and sofosbuvir are substrates of drug transporters P-glycoprotein (P-gp) and Breast Cancer Resistance Protein (BCRP) and may increase intestinal absorption of coadministered substrates for these transporters. P-gp inducers (e.g., rifampicin or St. John’s Wort) may decrease ledipasvir and sofosbuvir plasma concentrations, leading to reduced therapeutic effect of ledipasvir/sofosbuvir (Harvoni®), and the use with P-gp inducers is not recommended with ledipasvir/sofosbuvir (Harvoni®)

Clinically significant medicinal product interactions with ledipasvir/sofosbuvir (Harvoni®) mediated by cytochrome P450 enzymes (CYP450) or by uridine biphosphate glucuronosyltransferase (UGT) enzymes are not expected.

Due to effect on drug transporters, ledipasvir may also affect HMG- CoA Reductase Inhibitors (Statins). Details of individual interactions can be found in the SPC.

Further interactions specific to ledipasvir, are co-administration with acid reducing agents. Ledipasvir solubility decreases as pH increases. Medicinal products that increase gastric pH are expected to decrease concentration of ledipasvir. Therefore patients should be advised regarding timing and maximum doses of administration of ledipasvir/sofosbuvir (Harvoni®) and acid reducing medicines. Details can be found in the SPC and this may have relevance for patients purchasing OTC acid reducing medicines.

**Sofosbuvir/velpatasvir (Epclusa®)**

Sofosbuvir/velpatasvir (Epclusa®) is a fixed dose combination tablet containing sofosbuvir 400mg and velpatasvir 100mg and. Velpatasvir is a potent second generation NS5A HCV inhibitor. The NS5A protein is essential for viral assembly and replication. It is used in combination with sofosbuvir for treatment of all genotypes.

# Prescribing Information

Sofosbuvir/velpatasvir (Epclusa®)­ is indicated for treatment of chronic hepatitis C infection mono-infection and HCV/HIV-1 co-infection. The treatment regimen are dependent on both viral genotype and patient population.

Genotypes 1-6

* 1 tablet (100mg/400mg) taken by mouth once daily for 12 weeks
	+ ribavirin (weight based) may be added dependent on clinical circumstances
* For paediatric dosing and formulations, see summary of product characteristics.

Sofosbuvir/velpatasvir (Epclusa®) can be used in all stages of liver disease (ie non-cirrhotic to decompensated cirrhosis).

### **Administration**

The film-coated tablet is for oral use. Patients should be instructed to swallow the tablet whole. The film-coated tablet should not be chewed or crushed, due to the bitter taste of the active substance. The tablet should be taken with or without food.

**Missed doses**

Patients should be instructed that if vomiting occurs within 5 hours of dosing, an additional tablet should be taken. If vomiting occurs more than 5 hours after dosing, no further dose is needed.

If a dose is missed and it is within 18 hours of the normal time, patients should be instructed to take the tablet as soon as possible and then patients should take the next dose at the usual time. If it is after 18 hours then patients should be instructed to wait and take the next dose at the usual time. Patients should not be instructed to take a double dose.

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**Pregnancy +/- concomitant use with ribavirin**

There is limited data on use of sofosbuvir/velpatasvir (Epclusa®) in pregnancy. As a precautionary measure, the manufacturer does not recommend use in pregnancy.

When sofosbuvir/velpatasvir (Epclusa®) is used in combination with ribavirin, women of childbearing potential or their male partners must use two effective forms of contraception during the treatment and for a period of time after the treatment as recommended in the Summary of Product Characteristics for ribavirin.

**Effects on ability to drive and use machines**

sofosbuvir-velpatasvir (Epclusa®) has a negligible influence on the ability to drive and use machines. Patients should be informed that fatigue was more common in patients treated with sofosbuvir-velpatasvir (Epclusa®) than with placebo.

**Summary of safety profile**

Clinical trial data has shown that sofosbuvir/velpatasvir (Epclusa®) is well tolerated with the most common side effects reported are fatigue and headache.

**Drug-drug Interactions**

Consult the summary of product characteristics ([www.medicines.org.uk](http://www.medicines.org.uk)) or [www.hep-druginteractions.org](http://www.hep-druginteractions.org) for safety of concomitant meds or discuss with specialist clinical pharmacist.

The interaction profile for sofosbuvir/velpatasvir (Epclusa®) is similar to that of ledipasvir/sofosbuvir as detailed above and any interactions identified for sofosbuvir may occur with sofosbuvir/velpatasvir (Epclusa®).

Sofosbuvir and velpatasvir are substrates of drug transporters P-gp and BCRP and may increase intestinal absorption of coadministered substrates for these transporters. P-gp inducers (e.g., rifampicin or St. John’s Wort) may decrease sofosbuvir and velpatasvir plasma concentrations, leading to reduced therapeutic effect of sofosbuvir/velpatasvir (Epclusa®) and the use with P-gp inducers is not recommended with sofosbuvir/velpatasvir (Epclusa®).

Clinically significant medicinal product interactions with sofosbuvir/velpatasvir (Epclusa®) mediated by CYP450 or UGT enzymes are not expected.

Further interactions specific to velpatasivr, are co-administration with acid reducing agents. Velpatasvir solubility decreases as pH increases. Medicinal products that increase gastric pH are expected to decrease concentration of velpatasvir. Therefore patients should be advised regarding timing and maximum doses of administration of sofosbuvir/velpatasvir (and acid reducing medicines. Details can be found in the SPC but this may have relevance for patients purchasing OTC acid reducing medicines.

Due to effect on drug transporters, velpatasvir may also affect HMG- CoA Reductase Inhibitors (statins). Details of individual interactions can be found in the SPC.

**Glecaprevir/Pibrentasvir (Maviret®)**

Glecaprevir/pibrentasvir (Maviret®) is a fixed dose combination tablet containing glecaprevir 100mg and pibrentasvir 40mg. Glecaprevir is a NS3/4A protease inhibitor and pibrentasvir is a potent second generation NS5A HCV inhibitor.

# Prescribing Information

Glecaprevir/pibrentasvir (Maviret®) is indicated for treatment of chronic hepatitis C infection. The treatment regimen are dependent on both viral genotype and patient population.

Genotypes 1-6

* 3 tablets (300mg/120mg) taken by mouth once daily with or after food
	+ Non cirrhotics and cirrhosis (Compensated Childs A): 8 weeks
	+ Patients who are treatment experienced (pegylated-interferon/ribavirin +/- sofosbuvir) will require treatment for 8- 16 weeks dependent on clinical circumstances
* For paediatric dosing and formulations, see summary of product characteristics.

**Administration**

The film-coated tablet is for oral use. Patients should be instructed to swallow the tablets whole. The film-coated tablet should not be chewed or crushed, due to the bitter taste of the active substance. The tablets should be taken with or after food.

**Missed doses**

Patients should be instructed that if vomiting occurs within 3 hours of dosing, an additional tablet should be taken. If vomiting occurs more than 3 hours after dosing, no further dose is needed.

If a dose is missed and it is within 18 hours of the normal time, patients should be instructed to take the tablet as soon as possible and then patients should take the next dose at the usual time. If it is after 18 hours then patients should be instructed to wait and take the next dose at the usual time. Patients should not be instructed to take a double dose.

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**Pregnancy**

There is limited data on use of Glecaprevir/pibrentasvir (Maviret®) in pregnancy. As a precautionary measure, the manufacturer does not recommend use in pregnancy.

**Effects on ability to drive and use machines**

Glecaprevir/pibrentasvir (Maviret®) has a negligible influence on the ability to drive and use machines.

**Summary of safety profile**

Clinical trial data has shown that glecaprevir/pibrentasvir (Maviret®) is well tolerated with the most common side effects reported are fatigue and headache.

**Drug-drug Interactions**

**The following provides a brief overview.** Consult the summary of product characteristics (www.medicines.org.uk) , www.hep-druginteractions.org for safety of concomitant meds or discuss with specialist clinical pharmacist**.**

**Affect of glecaprevir/pibrentasvir on other medicines**

Glecaprevir and pibrentasvir are both inhibitors of the transporter BCRP, P-gp and organic anion transporting polypeptide family (OATP) 1B1/3. Therefore, medicines that are transported via these pathways maybe affected. A common example of this is statins. The maximum daily dose of these may need to be adjusted- see SPC for further information.

Glecaprevir and pibrentasvir are known to be a weak inhibitors of CYP3A, but no dose adjustments are required for CYP3A substrates when co-administered.

Co- administration of glecaprevir-pibrentasvir with ethinylestradiol can lead to increase in ALT and is not recommended.

**Affect of other medicines on glecaprevir-pibrentasvir**

Glecaprevir/pibrentasvir are substrates of CYP3A and various drug transporters including OATP1B, P-gp and BRCP. Co-administration of medicines which have the following affect are contraindicated

• inducers P-Gp decrease glecaprevir-pibrentasvir

• Inhibit OATP1B- increase glecaprevir

• Inducers of CYP3A

• Strong inhibitors of CYP3A

**Acid-reducing medications**

Further interactions specific to glecaprevir, are co-administration with acid reducing agents.. Medicinal products that increase gastric pH are expected to decrease concentration of glecaprevir. Therefore patients should be advised regarding timing and maximum doses of administration of glescaprevir-pibrentasvir and acid reducing medicines.

This may have relevance for patients purchasing OTC acid reducing medicines and details can be found in the SPC.

**Elbasvir/Grazoprevir (Zepatier®)**

Elbasvir/grazoprevir (zepatier®) is a co-formulated tablet containing elbasvir, a NS5A inhibitor plus grazoprevir a NS3 protease inhibitor, which has action against genotype 1 and 4.

In genotype 1a and 4, viral load +/- presence of NS5A polymorphisims- this is equivalent of resistance, will determine treatment regimen. Dependent on these results treatment may be extended and ribavirin added.

Prescribing information

|  |  |
| --- | --- |
| Genotype 1a + 4 Non-cirrhotic + compensated cirrhosis (Childs A only) Viral load < 800,000 IU/ml | elbasvir-grazoprevir 12 weeks\*G1a viral load >800,000 IU/ml + presence of presence of specific NS5A polymorphisms (equivalent to resistance)or G4 viral load >800,000 IU/mlelbasvir-grazoprevir for 16 weeks plus ribavirin |
| Genotype 1b Non-cirrhotic + compensated cirrhosis (Childs A only) | elbasvir -grazoprevir 12 weeks  |

**Administration**

Elbasvir/grazoprevir is taken as one tablet in the morning with or without food.

**Missed doses**

Elbasvir/grazoprevir can be taken within 16 hours. If more than 16 hours have passed since elbasvir/grazoprevir is usually taken, the missed dose should NOT be taken and the patient should take the next dose per the usual dosing schedule.

Patients should be instructed that if vomiting occurs within 4 hours of dosing, an additional tablet can be taken up to 8 hours before the next dose. If vomiting occurs more than 4 hours after dosing, no further dose is needed

**Pregnancy +/- concomitant use with ribavirin**

There is limited data on use of elbasvir/grazoprevir in pregnancy. As a precautionary measure, the manufacturer does not recommend use in pregnancy.

When elbasvir/grazoprevir is used in combination with ribavirin, women of childbearing potential or their male partners must use two effective forms of contraception during the treatment and for a period of time after the treatment as recommended in the Summary of Product Characteristics for ribavirin.

**Effects on ability to drive and use machines**

Elbasvir-grazoprevir +/- ribavirin is not likely to have an effect on the ability to drive and use machines. Fatigue has been reported during treatment with elbasvir/grazoprevir +/- ribavirin.

**Summary of the safety profile**

The most frequently reported adverse reactions were headache and fatigue. Further information about adverse effects can be found in the SPC.

### **Drug-drug-interactions**

Affect of elbasvir/grazoprevir on other medicines

Elbasvir and grazoprevir are both inhibitors of the transporter BCRP and grazoprevir inhibits P-gp. Therefore, medicines that are transported via these pathways maybe affected. A common example of this is statins. The maximum daily dose of these may need to be adjusted- see spc for further information.

Although grazoprevir is known to be a weak inhibitor of CYP3A, no dose adjustments are required for CYP3A substrates when co-administered.

Affect of other medicines on elbasvir/grazoprevir

Elbasvir-grazoprevir are substrates of CYP3A and various drug transporters including OATP1B, P-gp and BRCP. Co-administration of medcines which have the following affect are contraindicated

* inducers P-Gp decrease elbasvir-grazoprevir
* Inhibit OATP1B- increase grazoprevir
* Inducers of CYP3A
* Strong inhibitors of CYP3A

Consult the summary of product characteristics (www.medicines.org.uk) , [www.hep-druginteractions.org](http://www.hep-druginteractions.org) for safety of concomitant meds or discuss with specialist clinical pharmacist.

**Sofosbuvir/velpatasvir/voxilaprevir (Vosevi®)**

Sofosbuvir/velpatasvir/voxilaprevir (Vosevi®) is a fixed dose combination tablet containing sofosbuvir 400mg and velpatasvir 100mg and.voxilaprevir 100mg. Sofosbuvir is an NS5B polymerase inhibitor, velpatasvir is a potent second generation NS5A HCV inhibitor and voxilaprevir is an NS3 protease inhibitor.

# Prescribing Information

Sofosbuvir/velpatasvir/voxilaprevir (Vosevi®) is indicated for treatment of chronic hepatitis C infection mono-infection and HCV/HIV-1 co-infection. It has been approved by the SMC for use in Scotland for patients who:

1: Have failed to achieve a sustained virologic response (SVR) with a direct-acting antiviral (DAA)

or

2: Are DAA-naïve, have genotype 3 (GT3) infection, with or without cirrhosis, and are suitable for treatment with an eight-week course.

In NHS Lothian, sofosbuvir/velpatasvir/voxilaprevir (Vosevi®) is currently only used for DAA-experienced patients (genotypes 1-6), with or without cirrhosis, at the following dose/duration.

* 1 tablet (400mg/100mg/100mg) taken by mouth once daily for 12 weeks

Sofosbuvir/velpatasvir/voxilaprevir (Vosevi®) should not be used in patients with decompensated cirrhosis.

**Administration**

The film-coated tablet is for oral use. Patients should be instructed to swallow the tablet whole. The film-coated tablet should not be chewed or crushed, due to the bitter taste of the active substance.

The tablet should be taken with food.

**Missed doses**

Patients should be instructed that if vomiting occurs within 4 hours of dosing, an additional tablet should be taken. If vomiting occurs more than 4 hours after dosing, no further dose is needed.

If a dose is missed and it is within 18 hours of the normal time, patients should be instructed to take the tablet as soon as possible and then patients should take the next dose at the usual time. If it is after 18 hours then patients should be instructed to wait and take the next dose at the usual time. Patients should not be instructed to take a double dose.

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**Pregnancy**

There is limited data on use of sofosbuvir/velpatasvir/voxilaprevir (Vosevi®) in pregnancy. As a precautionary measure, the manufacturer does not recommend use in pregnancy.

**Effects on ability to drive and use machines**

Sofosbuvir/velpatasvir/voxilaprevir (Vosevi®) has a negligible influence on the ability to drive and use machines.

**Summary of safety profile**

Clinical trial data has shown that sofosbuvir/velpatasvir/voxilaprevir (Vosevi®) is well tolerated. The most common side effects reported are headache, diarrhoea and nausea.

**Drug-drug interactions**

Consult the SPC ([www.medicines.org.uk](http://www.medicines.org.uk)) or [www.hep-druginteractions.org](http://www.hep-druginteractions.org) for safety of concomitant meds or discuss with specialist clinical pharmacist.

Voxilaprevir is metabolised *in vitro* by CYP3A4 with the vast majority of drug in plasma being the parent drug. Velpatasvir and voxilaprevir are both inhibitors of drug transporters P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), organic anion-transporting polypeptide (OATP) 1B1 and OATP1B3. Co-administration of sofosbuvir, velpatasvir and voxilaprevir with medicinal products that are substrates of these transporters may increase the exposure of the co-medications. This means that those where elevated plasma levels are associated with serious events are contraindicated and others may require dose adjustment or additional monitoring.

Rosuvastatin is contraindicated (due to BCRP and OATP1B inhibition by voxilaprevir and velpatasvir) as there is a 19-fold increase in plasma exposure of the statin. As this effect is likely to be attributed more to the BCRP transporter, other drugs that are a BCRP substrate including methotrexate, mitoxantrone, imatinib, irinotecan, lapatinib, sulfasalazine and topotecan are also not recommended.

Caution is required with OATP1B inhibitors such as ciclosporin as voxilaprevir plasma exposure increases 19-fold, or with OATP1B substrates such as edoxaban as voxilaprevir inhibition is expected to increases the exposure of the factor Xa inhibitor. These combinations are both not recommended.

Concomitant use with medicinal products that are strong P-gp and/or strong cytochrome P450 (CYP) inducers such as rifampicin, rifabutin, St. John's wort, carbamazepine, phenobarbital or phenytoin are contraindicated due to the decrease in sofosbuvir, velpatasvir and/or voxilaprevir exposure with the potential loss in efficacy. However, there are also drugs that are moderate P-gp or CYP inducers (such as modafinil, efavirenz, oxcarbazepine and others) which can also reduce exposure of this DAA and currently these are also not recommended.

**In-direct acting antivirals**

### [**Ribavirin**](http://reference.medscape.com/drug/rebetol-ribasphere-ribavirin-342625)

* Ribavirin is an antiviral nucleoside analogue. Given alone, ribavirin has little effect on the course of hepatitis C. It is used in combination with the DAA drugs in certain patients depending on clinical circumstances such as genotype, previous treatment and presence of cirrhosis..). Dose is weight based . Usual dose ranges arePatients <75kg 1000mg/day in 2 divided doses
* Patients >75kg 1200mg/day in 2 divided doses

The majority of known side effects reported are from use in combination with PEG-interferon,. Common side effects with ribavirin are anaemia, rash, dry skin, GI disturbance. Other side effects reported from use with PEG-interferon include flu-like symptoms, low mood,fatigue and ophthalmic disturbance See summary of product characteristics for further information ([www.medicines.org.uk](http://www.medicines.org.uk))

Due to the teratogenic effects of ribavirin, women of childbearing potential or their male partners must use two effective forms of contraception during the treatment and for a period of time after the treatment as recommended in the Summary of Product Characteristics for ribavirin ([www.medicines.org.uk](http://www.medicines.org.uk))

**Community Supply of HCV Medication**

NHS Lothian has a commitment to deliver on the Scottish Government’s policy initiative “Shifting the Balance of Care”. The policy guidelines require improvements to health and social care services that improve the health and well-being of the population. In particular, changes are required so that the work of secondary care and primary care becomes more integrated and that care becomes located around community-based services. The development of new medicines, like those for HCV, has meant that many treatments have become available that transform previously fatal or debilitating diseases into conditions that a patient may manage successfully for many years. Realising the investment in the patient’s health requires that health services commit to normalising the patient’s experience of care as much as possible, through integration with standard primary-care services.

To achieve these aims for patients with HCV in Lothian the hospital based multidisciplinary team (MDT) led by the prescribing consultants will identify patients that fit the current guidelines for appropriate prescribing of the HCV agent. A start date (usually in 2 weeks time) will be agreed at pre- treatment visit, where the patient will also receive advice on their treatment and management of HCV. Tthe specialist MDT will make arrangements with the patient () for which community pharmacy they will attend. The specialist service will ensure prescription is legal and liaise with community pharmacist to allow seamless supply chain and cover of any issues that may arise. The specialist pharmacy team will provide all the suitable patient specific information and guidance to enable the community pharmacist to provide pharmaceutical care to the patient. The specialist pharmacy team will inform the community pharmacy when a prescription for the patient has been issued. The prescription will contain the patient’s community health index (CHI) number and an indication of whether there is a need for instalment dispensing its frequency and if supervision is required after a discussion with the community pharmacist.

The community pharmacist will order sufficient medication from the pharmaceutical company or their wholesaler to ensure continuous treatment of the patient. The community pharmacist will discuss the service they provide with the patient at presentation and consider if registration for the Chronic Medication Service is appropriate. The community pharmacist will provide suitable information and advice to the patient to enable them to take their medicines accurately and appropriately and to manage any adverse effects that they may experience. The community pharmacist will contact the specialist pharmacy team (or clinical nurse specialist when clinical pharmacist absent) during working hours if the patient is experiencing problems, stops treatment or fails to collect their treatment when they require a further supply.

The scope of items which may be dispensed by community pharmacy contractors through this specification will be subject to local board formulary advice. Inclusion in local board formulary will reflect existing good clinical practice and SMC advice.

**Contacts**

In NHS Lothian, services for Hepatitis C are provided by specialists based at either Regional Infectious Disease Unit, Western General Hospital or Liver Unit, Royal Infirmary of Edinburgh, often through outreach clinics at various locations across Lothian.

Contact Details for Specialist Services

Hepatitis C Services, Regional Infectious Disease Unit, Western General hospital

 0131 537 2820

Consultant

Dr Daire O’Shea

Associate Specialist

Dr Hazel Rae

BBV Clinical Nurse specialists 0131 537 2856

Sara Lamond

Fiona Rose

Jesse Ryan

Community BBV Team 0131 537 2820

Nurse specialists

Mina O’Hara

Jacky Shaw

Mark Quiletti-Bird

Outreach support workers

Laura Rodiguerz

Steven Scott

Hepatitis C Services, Hepatology, Royal Infirmary of Edinburgh

0131 252 1630

Consultants

Dr Andrew Bathgate

Professor Peter Hayes

Clinical nurse specialists

Kim MacBeth 0131 242 1639

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