Dr Jeffrey Ngu

Consultant Gastroenterologist and Hepatologist at Christchurch Hospital

Saturday, August 10, 2019

(Room 8)

7:00 - 7:55 AbbVie Breakfast Session - GPs Roles in Hep C Elimination

abbvie

MAVIRET®* FOR TREATMENT OF CHRONIC HEPATITIS C

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CLINICAL EDUCATION FOR GENERAL PRACTICE

*MAVIRET is a combination tablet containing glecaprevir and pibrentasvir

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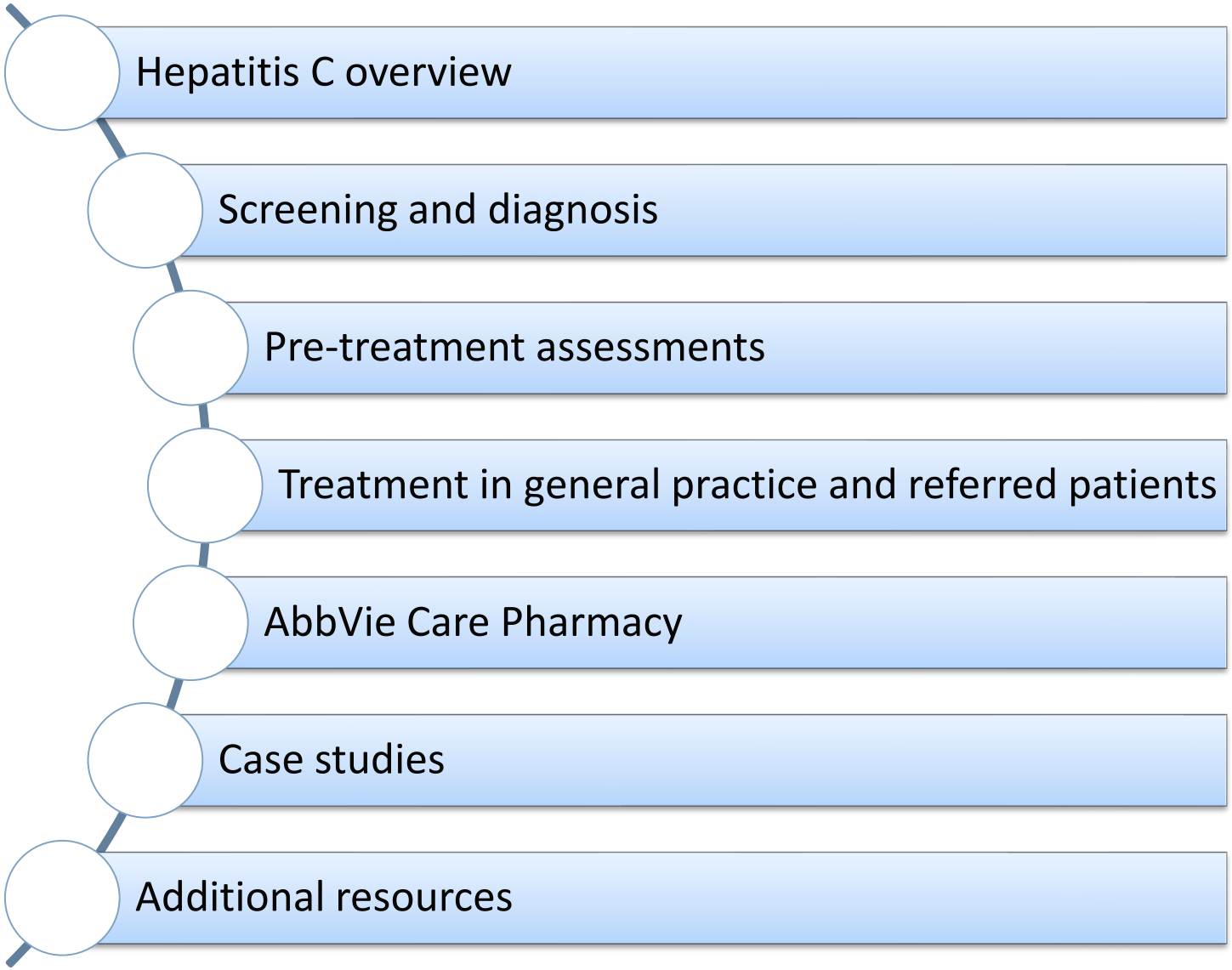
Overview of content



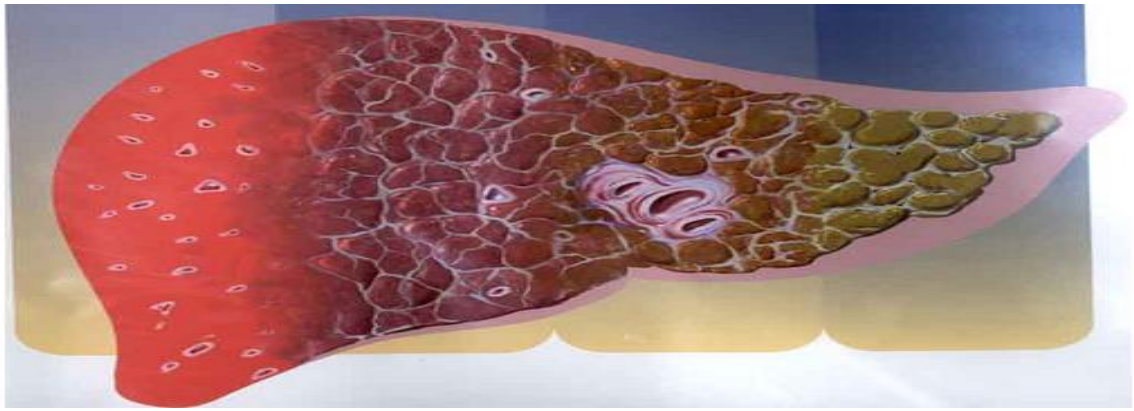
WHAT IS HEPATITIS C?

Overview of clinical information and key facts on prevalence and risk factors for infection in New Zealand

What is hepatitis C?

- The hepatitis C virus (HCV) is a blood-borne virus that infects the liver and causes inflammation.
- Infection with HCV is often undiagnosed as most people do not have symptoms.
- Acute infections can clear spontaneously in approximately 25% of patients.
- However, approximately 75% of cases progress to chronic hepatitis C, which can go undiagnosed for up to 20 to 30 years.
- If HCV is left untreated, chronic infection can damage the liver, and may progress to fibrosis, cirrhosis, liver failure, hepatocellular carcinoma (liver cancer), and death.

Inflammation and scarring of the liver
which may lead to fibrosis and cirrhosis.

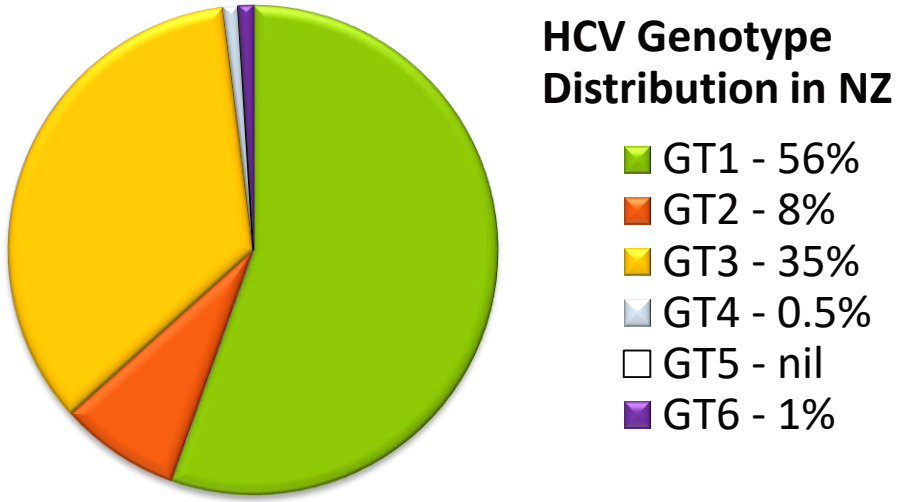


Progressive liver damage which may occur from infection with the hepatitis C virus

CDC. Hepatitis C Questions and Answers for the Public. Available at https://www.cdc.gov/hepatitis/hcv/cfaq.htm. Accessed July 2018.
Cacoub P, et al. Ther Adv Infect Dis 2016; Feb; 3(1): 3-14.

Chronic hepatitis C in New Zealand

- In NZ, 50,000 people are estimated to have chronic infection with the hepatitis C virus (HCV). Of these it is estimated only around 50% have been diagnosed.
  - It is estimated there are 1000 new infections per year
  - The median age of diagnosis is 47y and duration of infection is >25y
- Hepatitis C can be further categorized into 6 major genotypes (GTs) or strains



Gane E, et al. *NZ Med J* 2014;127(1407):61–74.
Ministry of Health. Hepatitis C. 2016 www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/hepatitis-c.

Risk factors for hepatitis C in New Zealand

The hepatitis C virus is spread through blood to blood contact.

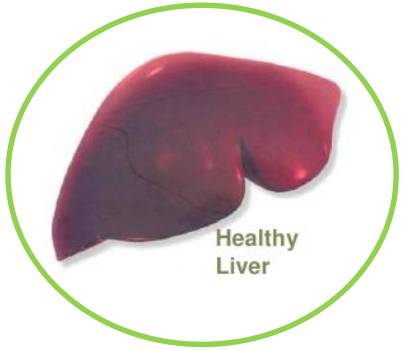
Key risk factors for hepatitis C infection in New Zealand include ever having:

- **injected drugs** and shared needles or equipment, even just once. Incidence of HCV infection was high in the 1960s-1980s secondary to the rise in recreational injecting drug use.
- had a **tattoo or body piercing** using unsterile equipment.
- had a **blood transfusion** in New Zealand before 1992, when blood screening for HCV began.
- **lived** or received **medical treatment** in a **country of high HCV prevalence** and suboptimal medical equipment sterilisation (e.g. South East Asia, India, the Middle East, or Eastern Europe).
- ever been in **prison**.
- been **born to a mother living with hepatitis C**. There is a 5% risk of HCV transmission of the HCV virus during birth and transmission also occasionally occurs within households. All children of women with chronic HCV should be tested once they are at least a year old.

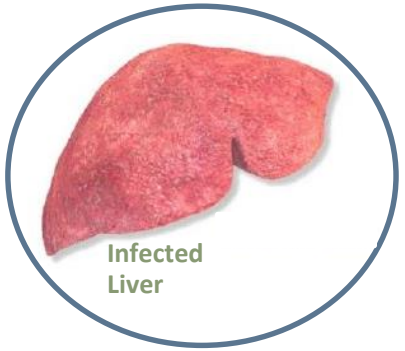
Gane E, et al. *NZ Med J* 2014;127(1407):61–74.
Hepatitis Foundation NZ, Who is at risk of having hepatitis C? https://www.hepatitisfoundation.org.nz/hepatitis-c/who-is-at-risk/ Accessed Aug 2018.

Hepatitis C progression

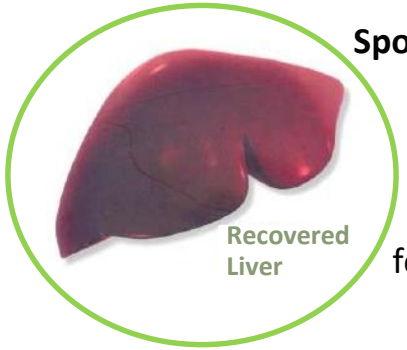
Exposure to Hepatitis C virus resulting in infection



Acute HCV



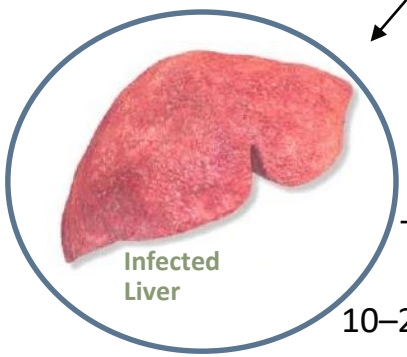
HCV cleared spontaneously in ~25% of cases



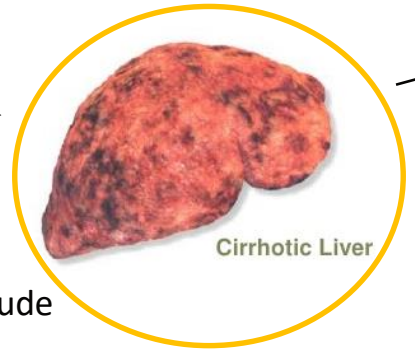
Spontaneous clearance

No acquired immunity; patients should be retested for HCV if risk factors remain

Progression to **chronic HCV** in ~75% of cases (most with no apparent symptoms)

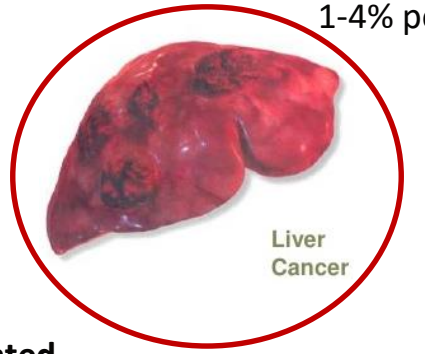


Cirrhosis
10–20% of patients over 20 years;
co-factors for progression include HIV, HBV, and alcohol use



Decompensated cirrhosis
Liver function is impaired. Serious signs of liver failure may occur. 5 year survival rate is about 50%

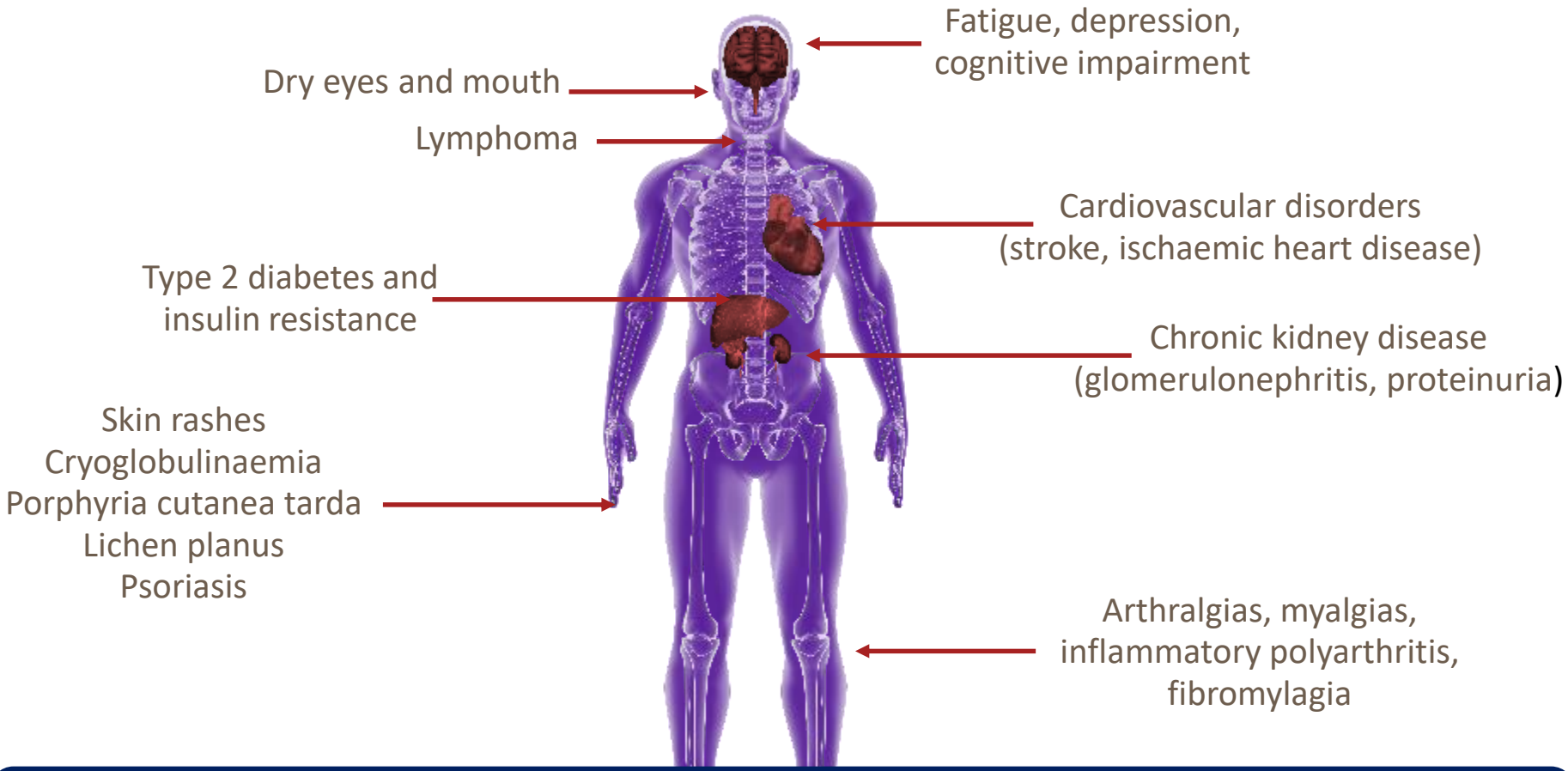
Hepatocellular carcinoma
1-4% per year



HCV=hepatitis C virus. HIV=human immunodeficiency virus. HBV=hepatitis B virus.

Chen S, Morgan T. The Natural History of Hepatitis C Virus (HCV) Infection. *Int J Med Sci* 2006; 3(2):47-52. Available at http://www.medsci.org/v03p0047.htm
Healthline. Cirrhosis and Hepatitis C: Their Connection, Prognosis, and More. Available at https://www.healthline.com/health/cirrhosis-and-hepatitis-c.

Extra-hepatic effects of hepatitis C



In many patients with chronic HCV, the virus can also cause negative effects beyond the liver, including cardiovascular, renal, metabolic, neurological, and immune diseases

Cacoub P, et al. Ther Adv Infect Dis 2016; Feb; 3(1): 3-14.
Garcovich S, et al. World J Hepatol. 2015 Nov 28; 7(27): 2740–2748.

SCREENING AND DIAGNOSIS

Identifying, testing, and diagnosing patients with hepatitis C

Which patients should be offered a test for HCV

It is recommended that **all patients with risk factors** for chronic HCV infection undergo testing.

Reminder of the risk factors:


Have used injectable drugs, even once


Received a blood transfusion or organ transplant prior to July 1992


Have migrated from or received a medical or dental intervention in a region with high HCV prevalence


Have spent time in prison

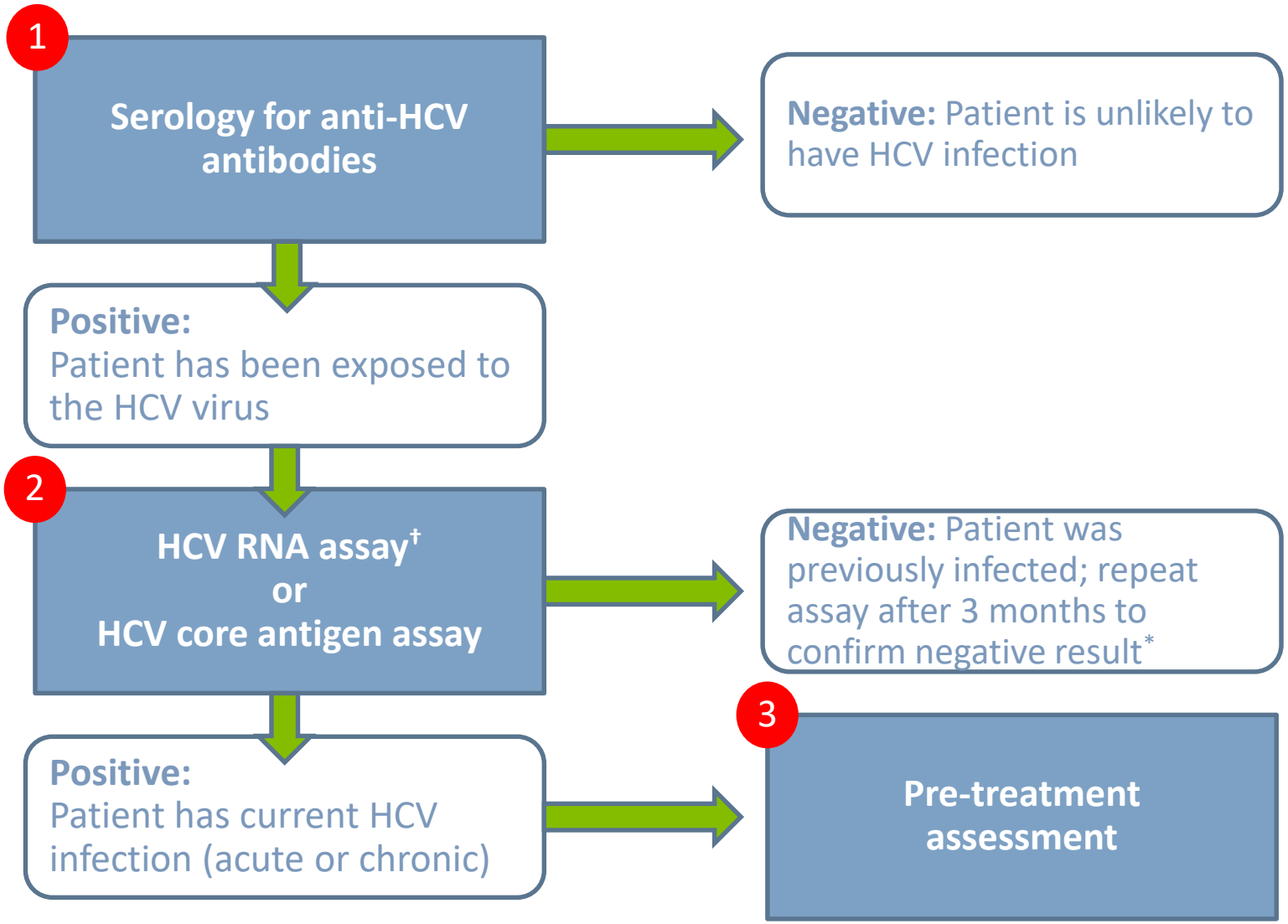

Have a tattoo, body piercing or alteration


Have a history of acute hepatitis, jaundice or persistently elevated ALT level


Were born to an HCV infected mother

Bpacnz. Hepatitis C: you can't treat it if you don't test for it. BPJ June 2017. https://bpac.org.nz/2017/hepc.aspx Accessed January 2019.

How to test for hepatitis C



†Some regions employ reflex testing for HCV RNA based on a positive antibody test. Check your local health pathway for more information.
*For patients diagnosed during the acute stage of infection, repeat testing after 3 months is recommended to confirm the negative result.

Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

PRE-TREATMENT ASSESSMENT

Key elements of HCV pre-treatment assessment

- Evaluate for the presence of cirrhosis
- Evaluate for the presence of hepatitis B virus (HBV) or human immunodeficiency virus (HIV) coinfection, or other major co-morbidities
- Consider whether coexisting liver diseases are present
  - Heavy alcohol intake
  - Fatty liver disease
  - Further investigations (e.g. iron studies) if indicated
- Evaluate renal function
- Consider concomitant medications for risk of drug–drug interactions
- Test for pregnancy and discuss the need for contraception
  - DAAs are not recommended for use in pregnant or lactating women
- Determine whether previous treatment for hepatitis C has been taken

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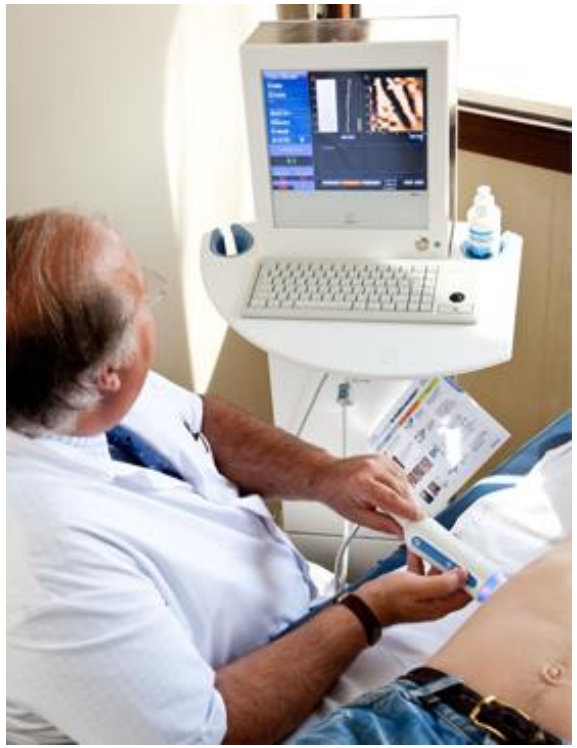
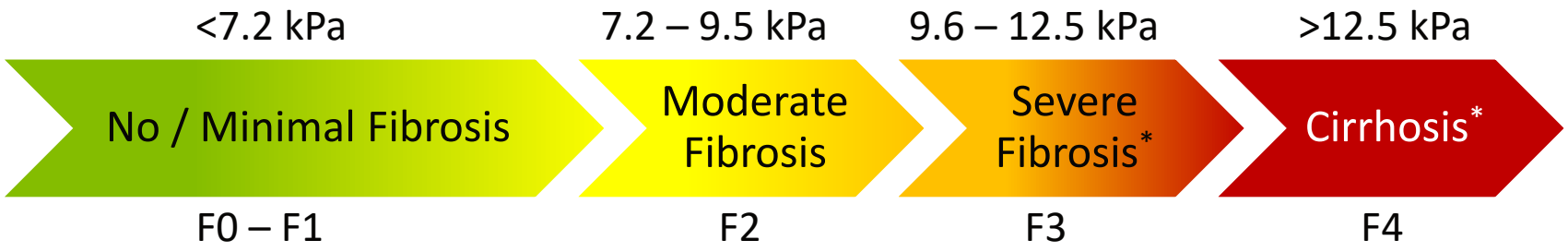
How to assess of fibrosis or cirrhosis

- Fibroscan® is non-invasive Transient Elastography (TE)
- Measures velocity of shear wave, correlates to tissue stiffness (liver fibrosis)



Understanding Fibroscan scores:

F0-F1	No/minimal fibrosis	Normal liver, no scarring
F2	Moderate fibrosis	Moderate liver scarring
F3	Severe fibrosis	Severe liver fibrosis with a high risk of cirrhosis
F4	Cirrhosis	Extensive liver fibrosis consistent with cirrhosis.



*Fatty changes in the liver (from BMI > 30 kg/m^2 & diabetes) can cause a higher Fibroscan score.

The Hepatitis Foundation of New Zealand Fibroscan Report For Hepatitis C. Available at: https://www.hepatitisfoundation.org.nz/wpcontent/uploads/2016/11/scorecardhepc.pdf Accessed Jan 2019.

Alternative assessment for cirrhosis

- In instances where a Fibroscan is unsuccessful or not readily available, serum biomarkers can be used to assess cirrhosis
  - A blood test including aspartate aminotransferase (AST)* and platelets should be taken
  - Calculate the AST to platelet ratio index (APRI) using an online calculator (www.mdcalc.com/ast-platelet-ratio-index-apri); if score >1.0 the patient is at significant risk of cirrhosis

$$\text{APRI} = \frac{\dfrac{\text{AST Level } (IU/L)}{\text{AST (Upper Limit of Normal) } (IU/L)}}{\text{Platelet Count } (10^9/L)} \times 100$$

- Low albumin, low platelet count, elevated serum bilirubin or high INR (>1.3) may suggest cirrhosis
- Clinical signs of chronic liver disease include:
  - Jaundice
  - Abdominal pain
  - Ascites and peripheral oedema
  - Spider naevi
  - Palmar erythema
  - Asterixis
  - Hepatomegaly and splenomegaly

*In some regions AST is not included in the standard panel for liver function tests (LFTs) therefore AST will have to be specifically requested in addition to LTFs.

Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

When referral to secondary care is recommended:

Pre-treatment assessment		Refer to specialist if:
Assess liver fibrosis	• Cirrhotic status determines length of treatment • Detect clinical and laboratory signs of chronic liver disease • Undertake non-invasive assessment of the liver (fibroscan, APRI)	• Patient has evidence of cirrhosis (fibroscan ≥12.5 kPa or APRI ≥ 1.0)
Detect other causes of liver disease	• Check for viral coinfection with hepatitis A and B; vaccinate if indicated • Heavy alcohol use • Fatty liver disease • Other studies as clinically indicated	• Co-infected with HBV • Uncertain results from testing for other liver pathology
Detect other major co-morbidities	• Check for viral co-infection with HIV • Renal disease • Mental health • Drug and alcohol use	• Co-infected with HIV • Renal impairment (eGFR <30 mL/min/1.73m^2)
Review previous HCV treatment	• Treatment duration will be influenced by genotype and prior HCV treatment experience	• Previously treated for HCV

APRI=AST to platelet ratio index. HCC=hepatocellular carcinoma. HBV=hepatitis B. HIV=human immunodeficiency virus. eGFR=estimated glomerular filtration rate. HCV=hepatitis C virus.

ASHM. Decision-making in HCV. V8 Oct 2018. Available at: https://www.ashm.org.au/products/product/978-1-920773-43-4.
Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

INTRODUCTION TO MAVIRET®

Basic information on the MAVIRET combination of glecaprevir/pibrentasvir, how it works, and special considerations for use

Formulation

Glecaprevir (GLE)
pangenotypic NS3/4A protease inhibitor

Pibrentasvir (PIB)
Pangenotypic NS5A inhibitor

Glecaprevir/pibrentasvir approval was based on clinical trial data in over 2,300 patients including placebo and active-controlled studies

Glecaprevir/pibrentasvir is a fixed-dose combination of glecaprevir, an HCV NS3/4A protease inhibitor, and pibrentasvir, an HCV NS5A inhibitor, and is indicated for the treatment of adults and adolescents 12 years and older with chronic HCV GT 1, 2, 3, 4, 5 or 6 infection without cirrhosis and with compensated cirrhosis (Child-Pugh A)

GT=genotype. HCV=hepatitis C virus. NS=non-structural protein.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

Indications, contraindications, and precautions

INDICATIONS

MAVIRET is indicated for the treatment of adults and adolescents aged 12 years and over with chronic HCV.

CONTRAINDICATIONS

MAVIRET is contraindicated:

- In patients with severe hepatic impairment (Child-Pugh C)
- With atazanavir containing products and rifampicin; hypersensitivity to the active substances or to any of the excipients.

PRECAUTIONS

- Risk of Hepatitis B virus (HBV) reactivation: cases of Hepatitis B virus (HBV) reactivation, including fatal cases, have been reported during and after treatment of HCV with DAAs in HBV/HCV co-infected patients.
- MAVIRET is not recommended in patients with moderate hepatic impairment (Child-Pugh B).
- MAVIRET contains lactose; patients with rare hereditary problems of galactose intolerance, the Lapp lactose deficiency, or glucose-galactose malabsorption should not take MAVIRET.
- Risk of symptomatic hypoglycaemia: Treatment with MAVIRET my cause improvement of liver function resulting in improved glucose metabolism by the liver. In diabetic patients, this could lead to improved glucose control. Close monitoring of blood glucose levels is recommended in diabetic patients to determine if dose adjustment anti-diabetes medication is required.

HCV=hepatitis C virus. GT=genotype. HIV=human immunodeficiency virus. HBV=hepatitis B virus. DAA=direct-acting antiviral

Dosing

Recommended oral dose is 3 tablets taken once daily with food

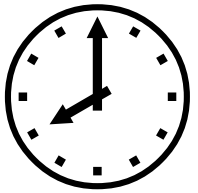
Daily blister sheet

Weekly carton

Monthly carton (28 Days)

Packaged: 7 x daily blister in weekly box
4 x weekly box in monthly box

- Tablets should be taken whole and not chewed, crushed or broken
- Blister packaging designed to aid adherence
- Missed doses, advice to patients:
  - If less than 18 hours from the usual time, take dose as soon as possible and take next dose at usual time
  - If more than 18 hours has passed, do not take missed dose and take the next dose at the usual time. Do not take a double dose



MAVIRET Data Sheet. Available at www.medsafe.govt.nz

MAVIRET* IN GENERAL PRACTICE

*Glecaprevir/pibrentasvir

Treatment duration

Recommended treatment duration for **treatment-naïve non-cirrhotic** patients

Patient populations	Recommended Treatment Duration
	No cirrhosis
TN GT 1,2,3,4,5 or 6	8 weeks

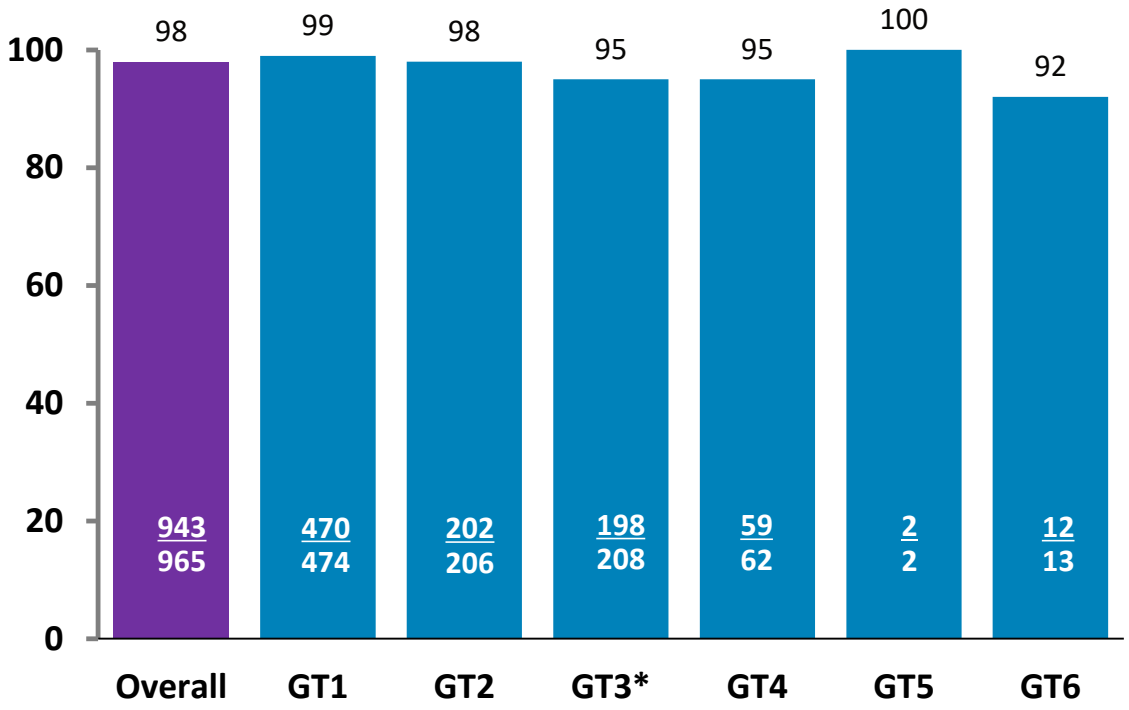
Dosage and durations are applicable to patients with:

- HCV/HIV-1 coinfection
- HCV/HBV co-infection - close monitoring is required for possible reactivation of hepatitis B during or after treatment for HCV
- Any stage of renal impairment including patients receiving dialysis

GT=genotype. TN=treatment-naïve. HCV=hepatitis C virus. HIV=human immunodeficiency virus. HBV=hepatitis B virus.

Efficacy – Treatment-naïve† non-cirrhotic patients with HCV GT1-6

MAVIRET for 8 Weeks (ITT)



High SVR12 rates were achieved with 8 weeks of MAVIRET in treatment-naïve non cirrhotic patients irrespective of HCV genotype and in GT 1, 2, 4, 5 and 6 patients experienced with prior PEG/RBV/SOF.

†GT 1, 2, 4, 5 and 6 patients includes patients experienced with prior regimens containing peginterferon (PEG), ribavirin (RBV), and/or sofosbuvir (SOF).
*GT 3 patients were all treatment-naive
HCV=hepatitis C virus. GT=genotype. ITT=intent-to-treat.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz
Puoti M et al. J Hepatol 2018; doi: 10.1016/j.hep.2018.03.007

Safety profile and common side effects

Fatigue, headache and nausea were the most common side effects observed.

Most adverse events were of **mild severity** across all trials

- The rate of adverse events in patients receiving MAVIRET (8, 12 or 16 weeks) was similar to those who received placebo
- The proportion of patients treated with MAVIRET who permanently discontinued treatment due to adverse events was 0.1%
- The type and severity of adverse events in patients with cirrhosis were overall comparable to those seen in patients without cirrhosis

Drug-drug interactions*

Contraindicated
Atazanavir
Rifampicin

***This is not an exhaustive list please refer to the full MAVIRET data sheet www.medafe.govt.nz & The University of Liverpool Hep Drug Interactions website www.hep-druginteractions.org.**

In some instances, the recommendations in the data sheet may differ to those on the University of Liverpool Hep Drug Interactions website.

Not Recommended *May lead to increased concentrations of MAVIRET*	
Ciclosporin >100mg	
Darunavir	
Lopinavir/ritonavir	
Not Recommended *May lead to reduced therapeutic effect of MAVIRET*	
Carbamazepine	
Efavirenz	
St John's Wort	
Not Recommended *May increase concentrations of co-administered drug*	
Atrovastatin†	Lovastatin†
Dabigatran	Simvastatin†
Not Recommended *Risk of ALT elevations*	
Ethinyloestradiol	

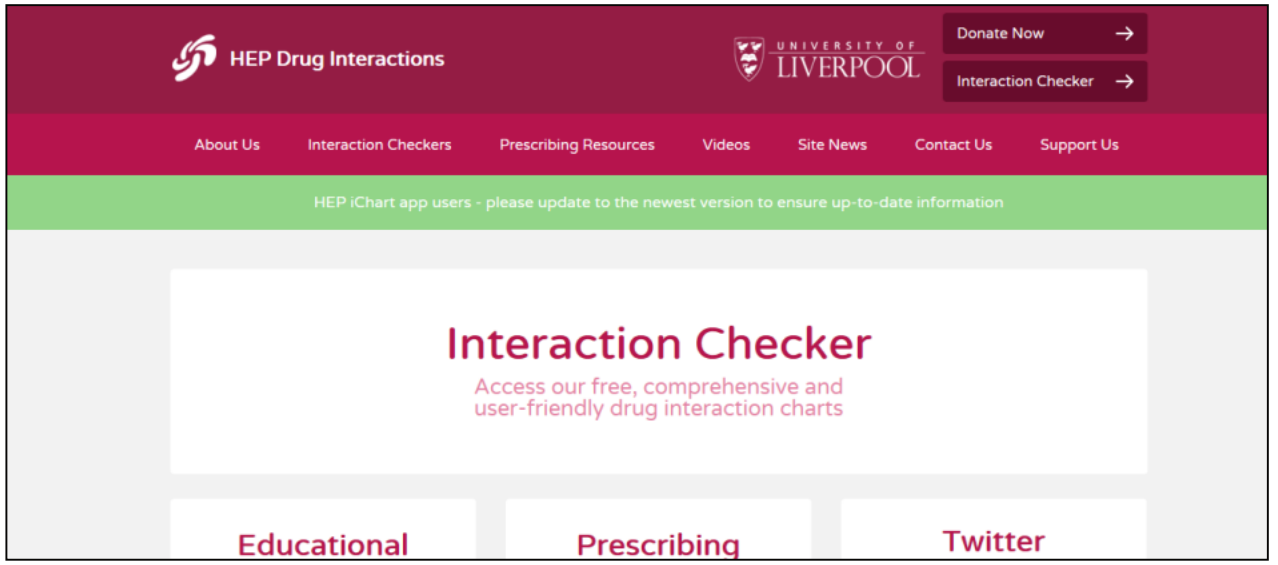
ALT=alanine aminotransferase.
†Increased statin concentrations may increase the risk of myopathy, including rhabdomyolysis.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz
University of Liverpool. HEP drug interactions. Available at: www.hep-druginteractions.org/.

Tools to support management of drug-drug interactions

1. **Medsafe-approved Data Sheet:** www.medsafe.govt.nz
   - Please first refer to the New Zealand label for all contraindicated medications, drug interactions, and precautions

2. **University of Liverpool website:** http://hep-druginteractions.org/
   - Searchable by alphabetical list of drugs (A-Z), by drug class, or by trade name
   - A mobile app is also available



Advice for patients during treatment

The following advice will help to give your patient the best chance of achieving cure[†] of their HCV infection:

Adherence is important; discuss strategies which will help individual patients

Tablets must be taken daily with food as directed; the type of food is not important; they can have a small snack or a full meal with their dose

Repeat monthly boxes of medication must be picked up from the pharmacist on time, to make sure there are no gaps in treatment

Avoid starting any new medicines during treatment (without consultation on potential drug interactions with their doctor or pharmacist)

Lifestyle changes such as reducing or eliminating alcohol consumption, cannabis use, and other illicit drug use, especially during treatment, may help to improve their liver health

[†]Cure, defined as HCV RNA below the lower limit of detection at 12 weeks post end-of-treatment (SVR12).

*Tablets images are for illustrative purposes only.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

On treatment monitoring

Follow up after 4 weeks of treatment is recommended to assess for adverse events and reinforce adherence

In non-cirrhotic patients treated in primary care, no blood tests are required during treatment

Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

Post treatment follow up

Check HCV RNA and Liver Function Tests (LFTs) 12 weeks after treatment has finished.

- Undetectable HCV RNA 12 weeks after treatment indicates a sustained virologic response (SVR12), or virologic cure.
- If HCV RNA is detected, the patient has not been cured and needs referral to secondary care or discuss with a gastroenterologist.
- Patients with normal liver function tests and without cirrhosis do not require additional follow-up. If LFTs are elevated despite sustained virologic response (SVR12), the patient requires further assessment for other causes of liver disease.
- Patients with cirrhosis before treatment should be referred to secondary care for long-term management and surveillance of hepatocellular carcinoma.
- **NOTE:** Patients with ongoing risk factors for HCV, such as continued injecting drug use, should be monitored for HCV infection with annual HCV RNA or HCV core antigen assays.

Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

Post treatment advice for patients

- **HCV antibodies will remain positive for life**, despite successful treatment.
- Cure does **NOT** protect against reinfection if re-exposed to hepatitis C.
- Harm reduction strategies will help to avoid reinfection.
- High risk activities that could lead to reinfection include:
  - sharing drug injecting or snorting equipment,
  - receiving a tattoo or body piercing with unsterilised equipment
  - sexual behaviours which may risk blood contact.

Bpacnz. Hepatitis C: you can't treat it if you don't test for it. BPJ June 2017. https://bpac.org.nz/2017/hepc.aspx Accessed April 2018.
ASHM. Hepatitis C. Your crucial role as a primary health care nurse. https://www.ashm.org.au/products/product/1-921850-24-8 Accessed Sept 2018.

MAVIRET® IN OTHER PATIENT POPULATIONS

Treatment experienced and cirrhotic patients

Recommended treatment duration for treatment-naïve patients with compensated cirrhosis

Patient populations	Recommended Treatment Duration
	Compensated cirrhosis
TN GT 1,2,3,4,5 or 6	12 weeks

Dosage and durations are applicable to patients with:

- HCV/HIV-1 co-infection
- HCV/HBV co-infection - close monitoring is required for possible reactivation of hepatitis B during or after treatment for HCV
- Any stage of renal impairment including patients receiving dialysis
- MAVIRET may be used for 12 weeks in liver or kidney transplant recipients

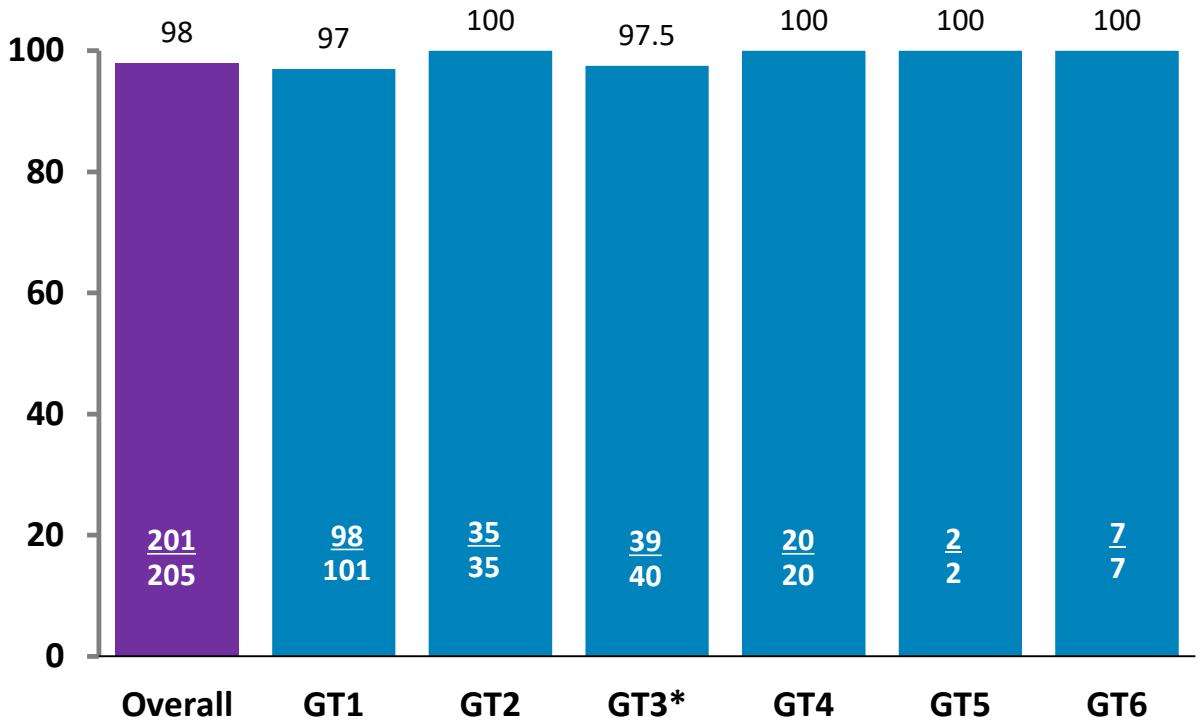
It is recommended that patients with cirrhosis are referred to secondary care

GT=genotype. TN=treatment-naïve. HCV=hepatitis C virus. HIV=human immunodeficiency virus. HBV=hepatitis B virus.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz
Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

Efficacy – Treatment-naïve* compensated cirrhotic patients with HCV GT1-6

MAVIRET for 12 weeks (ITT†)



High SVR12 rates were achieved with 12 weeks of MAVIRET in treatment-naïve compensated cirrhotic patients irrespective of HCV genotype and in GT 1, 2, 4, 5 and 6 patients experienced with prior PEG/RBV/SOF.

*GT 1, 2, 4, 5 and 6 TN patients includes patients experienced with prior regimens containing peginterferon (PEG), ribavirin (RBV), and/or sofosbuvir (SOF). †Includes patients who discontinued due to adverse events, lost to follow-up, or withdrew. HCV=hepatitis C virus. GT=genotype. ITT=intent-to-treat. SVR12=HCV RNA below the lower limit of detection at 12 weeks post end-of-treatment.

ABBVIE CARE PHARMACY PROGRAMME

Information and Logisitics

AbbVie Care Pharmacy Programme

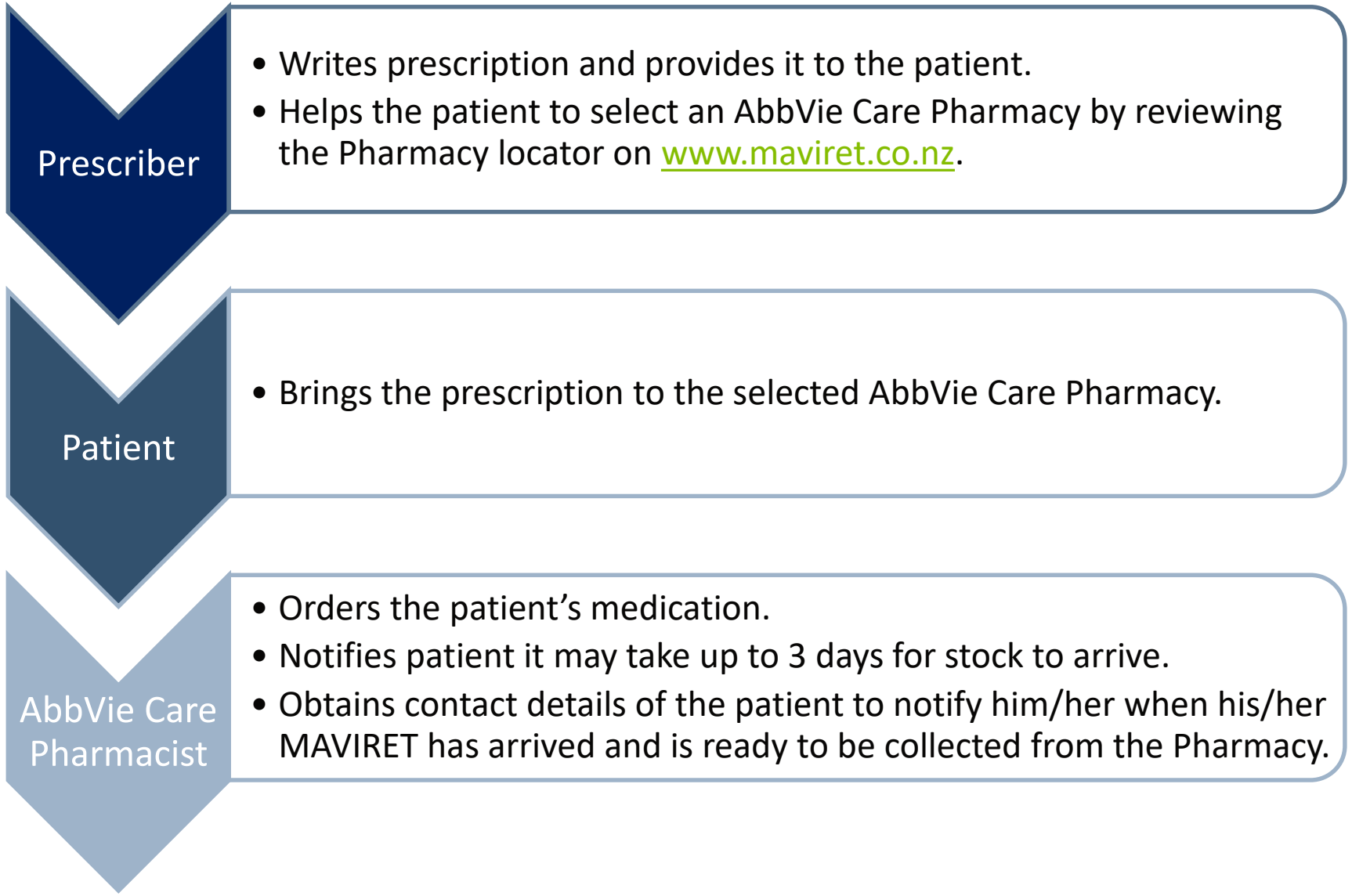
The AbbVie Care Pharmacy Programme (the **Programme**) is sponsored by AbbVie Limited (**AbbVie**), the manufacturer of MAVIRET® (glecaprevir/pibrentasvir).

The Programme connects pharmacists with adults who have been prescribed MAVIRET for the treatment of chronic hepatitis C.

MAVIRET is a fully funded prescription medicine on the Pharmaceutical Schedule from 1 February 2019 with an alternative XPHARM distribution arrangement.

- Under this XPHARM mechanism, the Pharmacy does NOT purchase the medicine and cannot claim a dispensing fee in relation to MAVIRET.
- Only pharmacies enrolled in the Programme can order and dispense MAVIRET.

AbbVie Care Pharmacy Programme



This is a simplified schema. For further details, see www.abbviecarepharmacy.co.nz

AbbVie Care Pharmacy Programme

AbbVie Care Pharmacist

- Receives the full treatment supply of medication from the supplier.
- Prepares medication for patient and contacts patient to collect.
- Informs patient that all repeats must be collected from the same pharmacy.†

Patient

- Collect their medication from the pharmacy, usually every 4 weeks.
- The patient does not pay a dispensing fee.
- Receives relevant information from the AbbVie Care Pharmacist when collecting their medication each month.

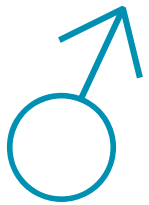
Prescriber

- Provides clinical support for the patient and advice to the pharmacist as required during treatment.

† Emergency supply is not an option.
This is a simplified schema. For further details, see www.abbviecarepharmacy.co.nz

PATIENT CASE STUDY #1

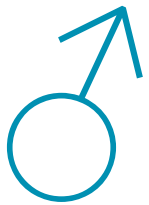
Case study: Stan



Stan is a patient you haven't seen for several years, as he feels has been healthy. He tells you his wife has insisted he come in to see you because of his fatigue, depression, and various skin rashes which seem to be getting worse. Stan's history is as follows:

Age	59 years
Social History	Married with 3 adult children Full time plumber Pack a day smoker since age 17, recently reduced to ½ pack per day Social drinker, 5-6 units of alcohol on weekends
Medical History	Knee replacement in 1986, requiring transfusion Increasing tiredness and fatigue over last 12 months Depressed mood for past 6 months Itchy rash on arms for approx 3 months, getting worse in past 2 weeks
Medications	Nil prescribed Taking supplements: Thiamine, St John's Wort, Magnesium, and Fish Oil

Case study: Stan

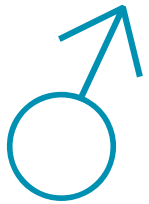


You do a physical assessment and order blood tests for Stan.
You include an **HCV antibody test** because **his symptoms could be related to hepatitis C**.
Stan also has a **risk factor** for hepatitis C as he had a **blood transfusion** in 1986.

Physical Assessment	Blood pressure: 135/82 Pulse: 64 Pruritic rash on the forearms and wrists consisting of groups of papules covered in fine, white reticular scales; likely lichen planus	
Blood test results	HCV antibody HBV antibody CRP ESR TSH Creatinine Bilirubin ALT Albumin Haemoglobin Platelets Prothrombin ratio	**Positive** Negative Not detected 18 mm/hr 2 mIU/L 1.1 mg/dL 17 µmol/L **47 IU/L** 38 g/L 146 g/L 191,000 cells/mm^3 1.0

HCV=hepatitis C virus. HBV=hepatitis B virus. CRP=C-reactive protein. ESR=erythrocyte sedimentation rate. TSH=thyroid stimulating hormone. ALT=alanine aminotransferase.

Case study: Stan



HCV Antibody test

This was **positive** so you call Stan back for confirmatory HCV testing.

HCV RNA test (PCR)

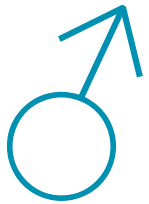
Stan has an HCV RNA blood test done with shows he has a **viral load of 1,215,422 IU/L** and confirms he has active hepatitis C infection.

Fibroscan

Stan needs to have the stage of his liver disease assessed in order to determine the correct MAVIRET treatment duration and whether or not he should see a specialist. Since Stan has never received HCV treatment before, an HCV genotype test is not necessary and will not impact which treatment duration he receives.

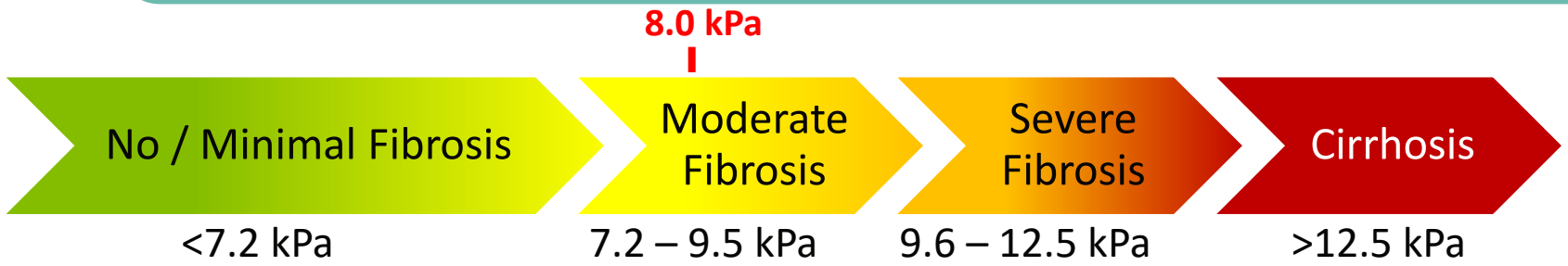
MAVIRET Data Sheet. Available at www.medsafe.govt.nz
Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

Case study: Stan



Stan's fibroscan result is 8.0 kPa.

The report states this is moderate fibrosis, F2.



Stan is not cirrhotic so you can treat him without a specialist referral. You plan to write Stan a prescription for 8 weeks of MAVIRET.

Patient populations	Recommended Treatment Duration
	No cirrhosis
TN GT 1,2,3,4,5 or 6	8 weeks

All patients with cirrhosis (Fibroscan ≥12.5kPa), should be referred to secondary care.

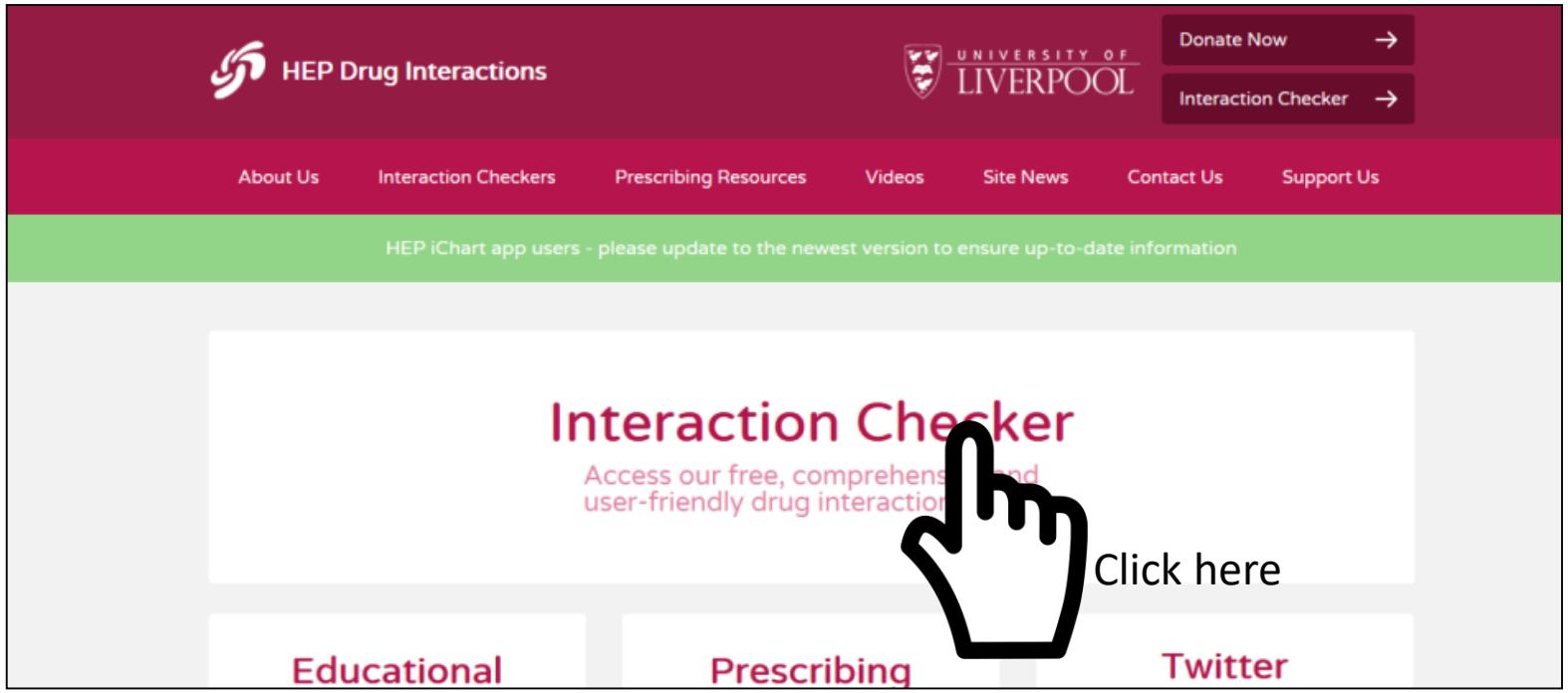
TN=treatment-naïve.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz
Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

Case study: Stan

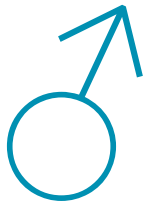
Medications	Nil prescribed Taking supplements: Thiamine, St John's Wort, Magnesium, and Fish Oil

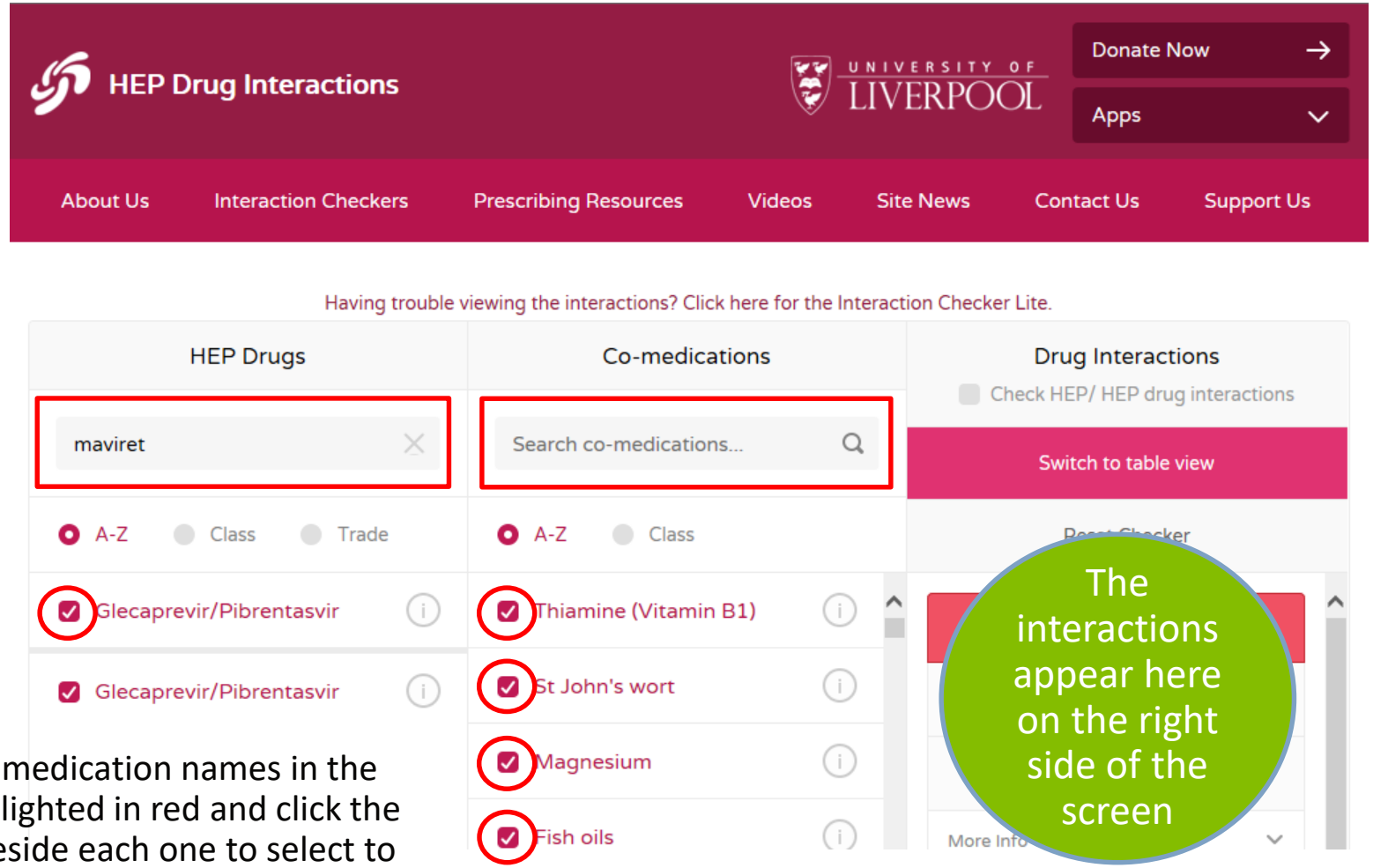
Stan is taking supplements, so you need to check to see if there are any interactions with MAVIRET prior to writing his prescription



University of Liverpool website: http://hep-druginteractions.org/

Case study: Stan





Type the medication names in the boxes highlighted in red and click the tick box beside each one to select to be included in the interaction report

University of Liverpool website: http://hep-druginteractions.org/

Case study: Stan

Entering Stan's medications on the Hep Drug Interactions website reveals the following information.

Stan must stop taking St John's Wort while he is taking MAVIRET

No Interaction Expected
Glecaprevir/Pibrentasvir
Thiamine (Vitamin B1)

No Interaction Expected
Glecaprevir/Pibrentasvir
Magnesium

No Interaction Expected
Glecaprevir/Pibrentasvir
Fish oils
More Info

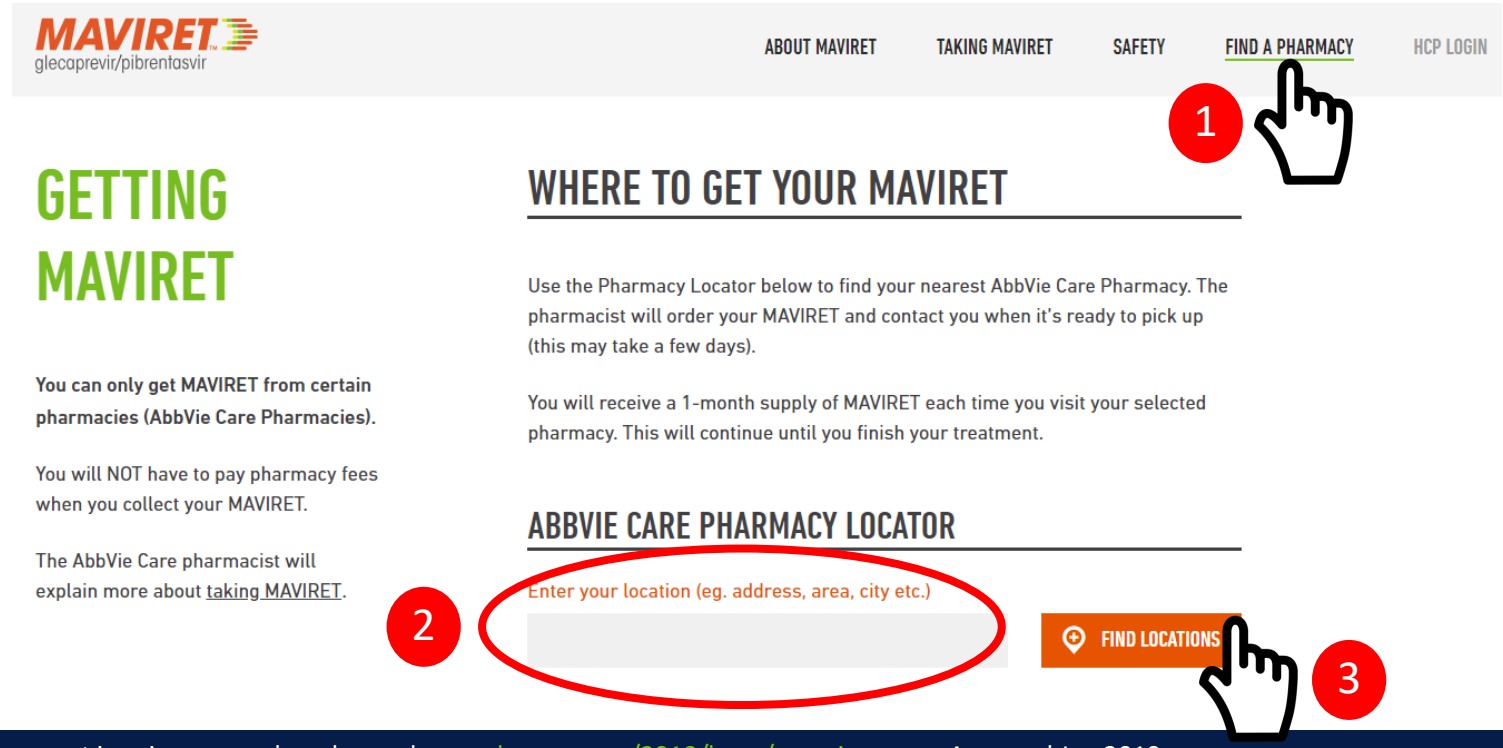
Do Not Coadminister
Glecaprevir/Pibrentasvir
St John's wort
More Info

Summary:
Coadministration has not been studied and is not recommended. Coadministration may decrease concentrations of glecaprevir/pibrentasvir which may lead to reduced therapeutic effect of glecaprevir/pibrentasvir.

University of Liverpool website: http://hep-druginteractions.org/

Case study: Stan

Stan agrees to stop taking the St John's Wort while he is on treatment.
You write him a prescription for an 8 weeks course of MAVIRET and help him to choose the AbbVie Care Pharmacy nearest to him using the **www.maviret.co.nz** website.
You also give Stan a blood test form for HCV RNA and LFTs and instruct him to get these tests done 3 months (12 weeks) after he takes the last dose of treatment to check for cure.

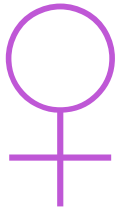


LFT=liver function tests.

Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

PATIENT CASE STUDY #2

Case study: Rosanna



Roseanna was diagnosed with hepatitis C in 2004, following getting clean from injecting drugs. She's been coming to your practice for the past 10 years now and you know her well.
Her history is as follows:

Age	39 years
Social History	Currently unemployed Lives in a flatting situation History of IVDU in the early 2000's, but clean since 2004 when she was diagnosed with hepatitis C Uses cannabis several times a week
Medical History	HCV genotype 3, never treated Moderate fibrosis (Fibroscan 7.4 kPa last year) On stable OST since 2004 Depression
Medications	Escitalopram 10mg OD Methadone 50mg OD (daily pick up) Levlen ED® 1 tab OD

Case study: Rosanna

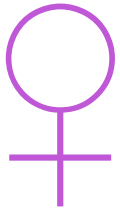
Rosanna has asked to be treated with the new hepatitis C treatment she heard about on the news, but she's worried about the side effects.
A friend of hers took a one year treatment of injections for hep C and got really sick a few years ago.

You reassure Rosanna that the new treatment is tablets only and discuss the common side effects and their management with her.

In clinical trials, most adverse events were of **mild severity** and only 0.1% of patients discontinued treatment due to an adverse event.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

Case study: Rosanna



HCV testing

Rosanna has already been tested and diagnosed with HCV. There is an HCV RNA test on file with a viral load of **800,436 IU/L** from last year.

Fibroscan

Rosanna's Fibroscan result last year was 7.4 kPa; she is not cirrhotic.
She is also known to be HCV genotype 3.

Patient populations	Recommended Treatment Duration
	No cirrhosis
TN GT 1,2,3,4,5 or 6	8 weeks

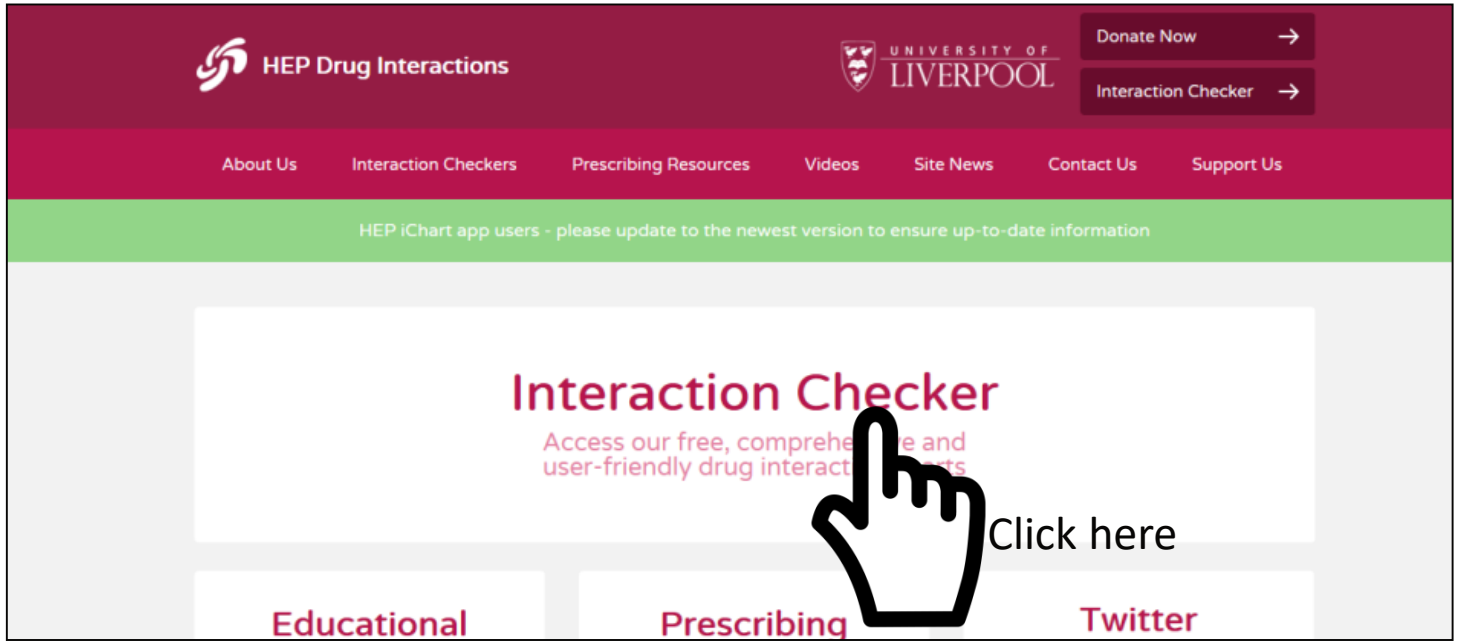
HCV=hepatitis C virus. TN=treatment-naïve.
MAVIRET Data Sheet. Available at www.medsafe.govt.nz

Case study: Rosanna

Medications	Escitalopram 10mg OD Methadone 50mg OD (daily pick up) Levlen ED® 1 tab OD
Other drugs	Cannabis

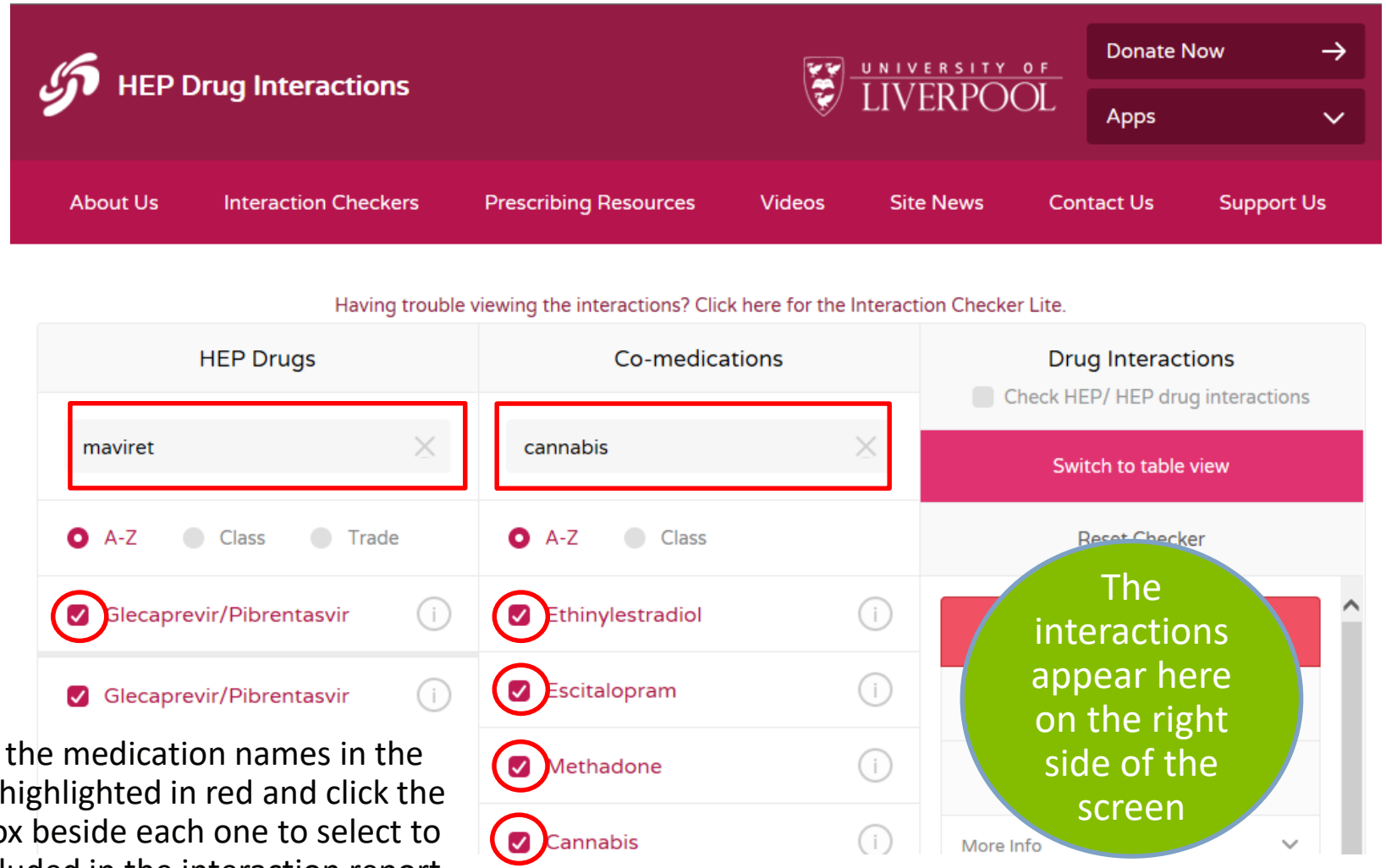
You must check for interactions with MAVIRET.

NB: Levlen ED® contains 30 micrograms ethinylestradiol and 150 micrograms levonorgestrel



University of Liverpool website: http://hep-druginteractions.org/

Case study: Rosanna



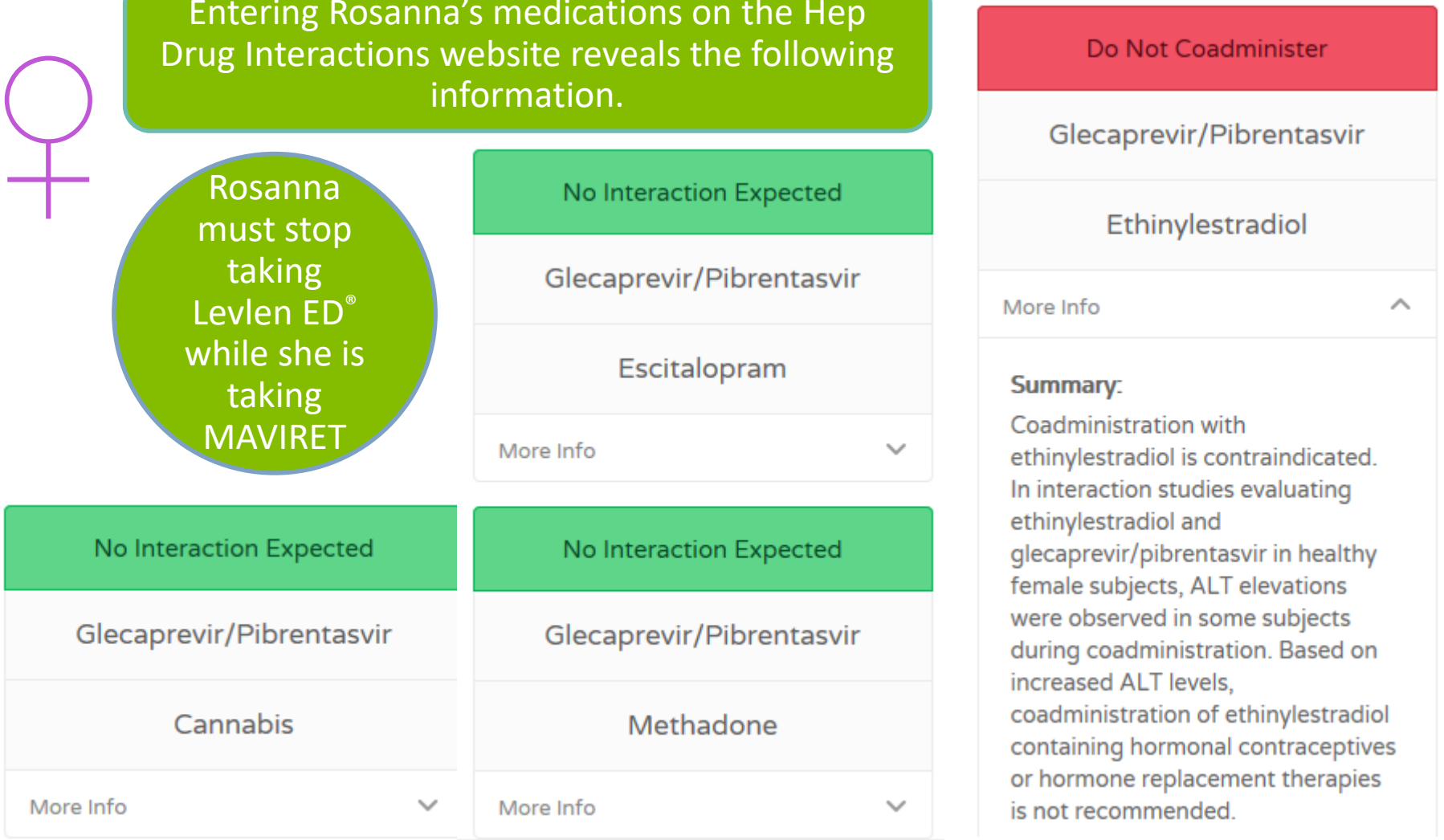
Type the medication names in the boxes highlighted in red and click the tick box beside each one to select to be included in the interaction report

University of Liverpool website: http://hep-druginteractions.org/

Case study: Rosanna

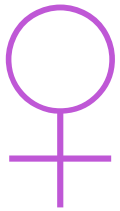
Entering Rosanna's medications on the Hep Drug Interactions website reveals the following information.

Rosanna must stop taking Levlen ED® while she is taking MAVIRET



University of Liverpool website: http://hep-druginteractions.org/

Case study: Rosanna



Rosanna agrees to stop taking Levlen ED® so she can take MAVIRET safely.

You discuss with her that use of MAVIRET is not recommended in pregnant women and therefore she should use another form of contraceptive while taking MAVIRET.

Following some discussion of the options, Rosanna agrees to have a non-hormonal copper IUD inserted.

Pregnant female patients, or those trying to become pregnant

- There is no data from the use of MAVIRET in pregnant women. As a precautionary measure, **MAVIRET use is not recommended in pregnancy.**
- Animal studies with glecaprevir or pibrentasvir do not indicate direct harmful effects on reproductive toxicity. Maternal toxicity in the rabbit precluded evaluation of glecaprevir at clinical exposures.

IUD=intrauterine device
MAVIRET Data Sheet. Available at www.medsafe.govt.nz

Case study: Rosanna

You get a call from Rosanna's pharmacist who sees her for daily methadone dispensing. He lets you know that Rosanna has reported nausea after taking her tablets since the first week of treatment.

The pharmacist has reported the adverse event and reinforced the need for Rosanna to take her tablets with food. He also suggested she take them with lunch instead of breakfast to see if that made a difference.

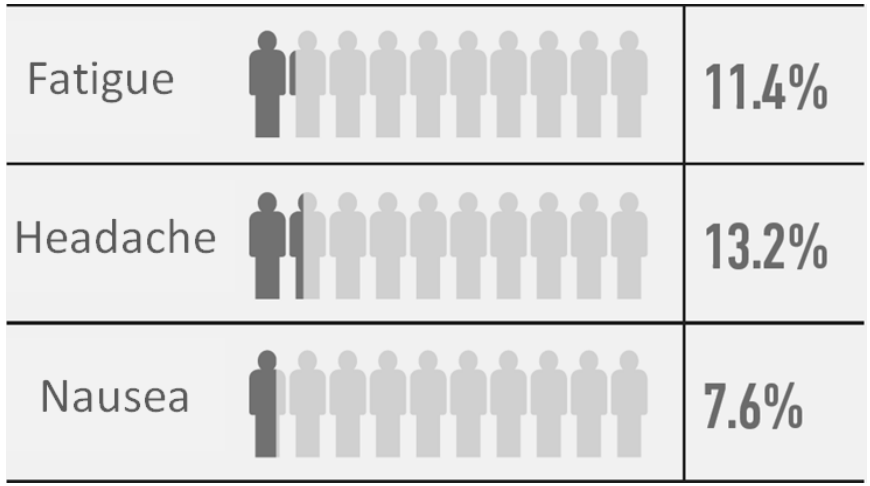
Ten days later the nausea persists.

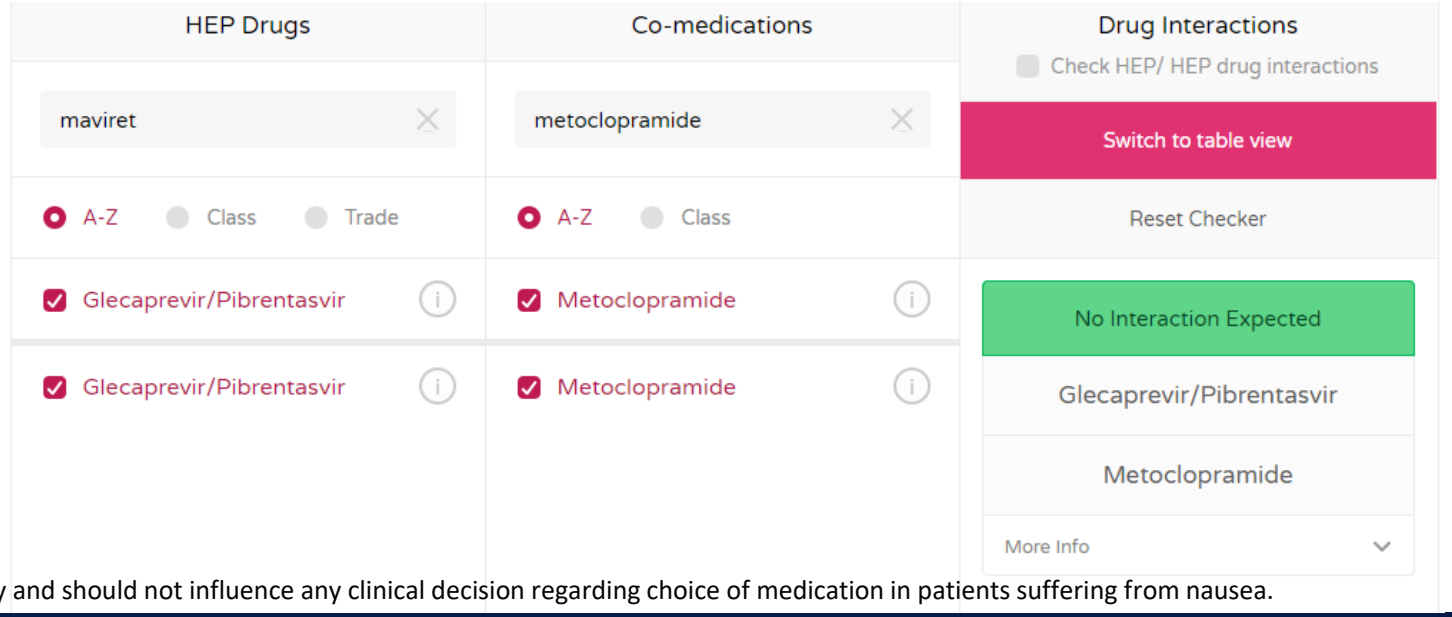
MAVIRET Data Sheet. Available at www.medsafe.govt.nz

Case study: Rosanna

You know that nausea is one of the common side effects of MAVIRET.

Since other strategies haven't worked for Rosanna, you write her a script for metoclopramide* and fax it to the pharmacy.

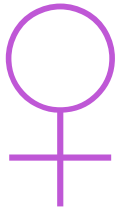




*This is an example only and should not influence any clinical decision regarding choice of medication in patients suffering from nausea.

MAVIRET Data Sheet. Available at www.medsafe.govt.nz
University of Liverpool website: http://hep-druginteractions.org/

Case study: Rosanna



Rosanna comes to see you during week 7 of treatment because she has been having flu-like symptoms for the past three days.

She's been taking paracetamol and ibuprofen as recommended by the pharmacist but has been getting worse. This morning she woke with a fever and muscle weakness.

You recommend usual care for flu-like illness including continuing the medications from the pharmacist, rest, and fluids.

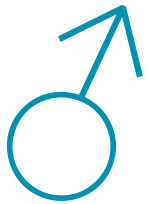
Reinforce to Rosanna that even though she isn't feeling well, she should continue to take the rest of her MAVIRET treatment.

Remember to report the adverse event to Abbvie at anzpv@abbvie.com and CARM at carmnz@otago.ac.nz

University of Liverpool website: http://hep-druginteractions.org/
MAVIRET Data Sheet. Available at www.medsafe.govt.nz

PATIENT CASE STUDY #3

Case study: David

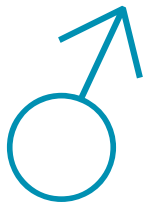


David has recently enrolled in your practice, having recently moved to your rural area from Christchurch.

He has known hepatitis C and heard the announcement that there are new medications available to be prescribed by GPs.

Age	49 years
Social History	Stable relationship with partner Nil current alcohol or illicit drugs
Medical History	HCV G3 diagnosed 14 years ago HCV treatment naïve Mild renal impairment
Medications	Nil

Case study: David



You find out that David hasn't been followed up for his hepatitis C for about 10 years. At the time he wasn't able to attend appointments and was discharged from the specialist clinic for DNAs.

Your physical assessment and David's laboratory results reveal the following:

Physical Assessment	Blood pressure: 122/84 Pulse: 70 Abdomen soft and non-tender Nil jaundice or oedema	
Blood test results	HCV RNA HBV antibody HIV antibody Creatinine Bilirubin ALT AST Albumin Haemoglobin Platelets Prothrombin ratio	**Positive** Negative Negative 1.1 mg/dL 17 µmol/L **47 IU/L** **58 IU/L** 38 g/L 146 g/L **144 10^9/L** 1.1

DNA=did not attend

Case study: David

Since there is no local Fibroscan clinic, you make sure AST and platelets are included in your laboratory tests so you can check to see if David might have cirrhosis using the APRI score.

$$\text{APRI} = \frac{\text{AST Level (IU/L)}: 58}{\text{AST (Upper Limit of Normal) (IU/L)}: 40} \times 100 = \frac{\text{Platelet Count } (10^9/L): 144}{} \times 100 = 1.007$$

Because David's APRI score is ≥1.0, he should be referred for a Fibroscan to confirm the presence or absence of cirrhosis.

You discuss this with David and refer him to the local gastroenterology department for a Fibroscan per your local health pathway.

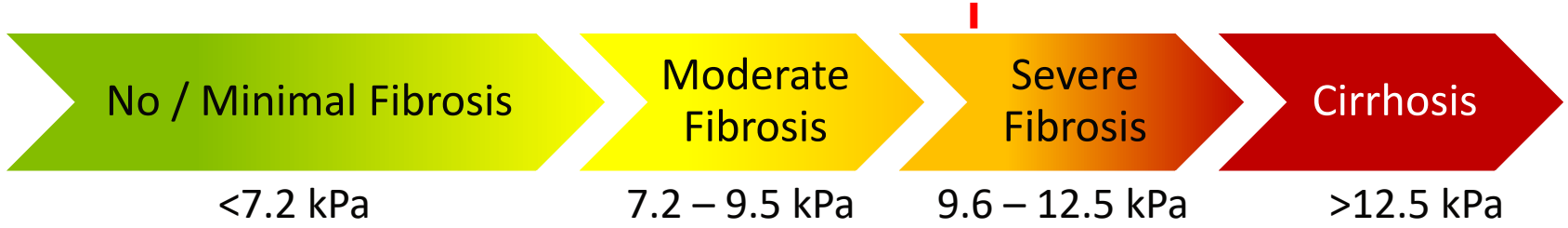
All patients with **APRI ≥1.0**, should be referred for a Fibroscan to confirm the presence or absence of cirrhosis.

Bpacnz. Hepatitis C management in primary care has changed. www.bpac.org.nz/2019/hepc/overview.aspx. Accessed Jan 2019.

Case study: David

David's fibroscan result is 9.8 kPa.

The report says this means he has severe fibrosis, F3.



David is confirmed as not cirrhotic so you can treat him without a specialist referral. You plan to write David a prescription for 8 weeks of MAVIRET.

Patient populations	Recommended Treatment Duration
	No cirrhosis
TN GT 1,2,3,4,5 or 6	8 weeks

All patients with cirrhosis (Fibroscan ≥12.5kPa), should be referred to secondary care for assesment.

TN=treatment-naïve

MAVIRET Data Sheet. Available at www.medsafe.govt.nz

ADDITIONAL RESOURCES

Links and resources

- AbbVie's disease awareness website for consumers www.hepcinfo.co.nz
- MAVIRET website www.maviret.co.nz
  - The user name and password for the HCP section are both GT1-6
  - Please refer to the pharmacy locator on www.maviret.co.nz with your patient to decide on the most convenient pharmacy location
- The Hepatitis Foundation of NZ www.hepatitisfoundation.org.nz/hepatitis-c/
- Ministry of Health NZ www.health.govt.nz/our-work/diseases-and-conditions/hepatitis-c and www.health.govt.nz/your-health/conditions-and-treatments/diseases-and-illnesses/hepatitis-c
- Best Practice Advocacy Centre New Zealand (bpac^{nz}) www.bpac.org.nz
- Community Alcohol and Drug Services www.cads.org.nz
- New Zealand Needle Exchange Programme www.nznep.org.nz

MAVIRET is a fully funded prescription medicine on the Pharmaceutical Schedule with an XPHARM distribution arrangement.
Please review approved Data Sheet before prescribing. This is available at www.medsafe.govt.nz.

MAVIRET® (glecaprevir 100 mg/pibrentasvir 40 mg) tablets. Prescription medicine. Please review full data sheet before prescribing. This is available from Medsafe at **www.medsafe.govt.nz**, or phone 0800 900 030. **INDICATIONS** MAVIRET is indicated for the treatment of adults and adolescents 12 years and older with chronic hepatitis C virus (HCV). **CONTRAINDICATIONS** Hypersensitivity to active substances or excipients; severe hepatic impairment (Child-Pugh C); concomitant use with atazanavir and rifampicin.
PRECAUTIONS Risk of Hepatitis B virus reactivation; not recommended in patients with moderate hepatic impairment (Child-Pugh B); patients with lactose intolerance; risk of hypoglycaemia in diabetic patients; pregnancy; lactation; safety and efficacy of MAVIRET in patients younger than 12 years of age have not been established. See data sheet for details. **INTERACTIONS** Potential for significant drug interactions requiring dose adjustment of the following medicines administered concomitantly: atorvastatin, carbamazepine; ciclosporin; dabigatran etexilate; darunavir; digoxin; efavirenz; ethinyloestradiol-containing products; lopinavir; lovastatin; pravastatin; ritonavir; rosuvastatin; St John's wort (Hypericum perforatum); simvastatin; Vitamin K antagonists. See data sheet for details. **ADVERSE EFFECTS** Headache, fatigue, nausea, serum bilirubin elevations. See data sheet for additional information on adverse effects in special populations. **DOSAGE AND ADMINISTRATION** The recommended oral dosage of MAVIRET in adults and adolescents 12 years and older is three glecaprevir/pibrentasvir 100 mg/40 mg tablets (total daily dose: glecaprevir 300 mg and pibrentasvir 120 mg) once daily with food. See data sheet for additional information on duration of treatment and use in special populations. **DATE OF PREPARATION** 20 June 2019, Version 5

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