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Saturday, June 10, 2017

7:00 - 7:55 Abbvie Breakfast Session

1. A Brighter Future for Your Hep C Patients
2. Ankylosing Spondylitis – Don't turn your back on it

A brighter future† for your Hep C patients – achieving cure in General Practice

Ed Gane, Auckland City Hospital

†Patients who achieve sustained virological response 12 weeks after end of treatment (SVR12) have substantially improved qualities of life, including physical, emotional, and social health[1]
*Cure is defined as undetectable HCV RNA 12 weeks following completion of treatment

1 American Association for the Study of Liver Diseases, Infectious Diseases Society of America. Recommendations for testing, managing, and treating hepatitis C. Available at www.hcvguidelines.org

Disclaimer

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AbbVie Ltd, Wellington. June 2017.
NZ-HCV-0065.

Disclosures

I am a member of the Advisory Board or Speakers Bureau for AbbVie, Alios, Alnylam, Arbutus, Arrowhead, Assembly, Gilead Sciences, Janssen, Merck, Mylan, and Roche.

The opinions expressed are my own.

AGENDA

TOPIC	LENGTH
1. Who should we test for hepatitis C	5’
2. Why we should treat hepatitis C	5’
3. Treatments for hepatitis C: prescribing and monitoring guidelines	10’
4. Treatments for hepatitis C: management of drug interactions	5’
5. Conclusions/Q&A	5’

Who should we test for hepatitis C?

Who is at risk for HCV infection?

1. Injecting drug use
   - In NZ, ~90% of transmission of HCV occurs this way
   - Peak age of infection 15–25 years
   - Peak incidence 1970–1990

2. Transmission through blood transfusions
   - Blood products have been screened for HCV since 1992
   - Immigrants from countries where HCV is endemic may have been exposed from vaccinations, hospital care

Total number infected >50,000
Estimated undiagnosed = 40–50%

Gane E, et al. *NZ Med J* 2014;127(1407):61–74.

Who is at risk for HCV infection?

3. Few infected via unsafe tattooing, body piercing, or contact with blood via other activities (sporting, violence, or occupational)

4. Mother-to-child transmission in 5%
   - No impact of mode of delivery
   - Test all children of HCV+ women
   - Wait until >12 months (maternal anti-HCV)

Anyone with a history of jaundice or abnormal liver function should consider a test, particularly if they also have other risk factors.

Hepatitis C – 7 key questions

1. Have you ever injected drugs?
2. Have you received blood transfusion prior to 1992?
3. Have you ever been in prison?
4. Have you ever had jaundice or abnormal liver function?
5. Have you ever lived in or received health care in SE Asia, Indian subcontinent, Middle East, Eastern Europe?
6. Does your mother or household member have HCV?
7. Have you ever received a tattoo or body piercing using unsterile equipment?

Hepatitis C tests

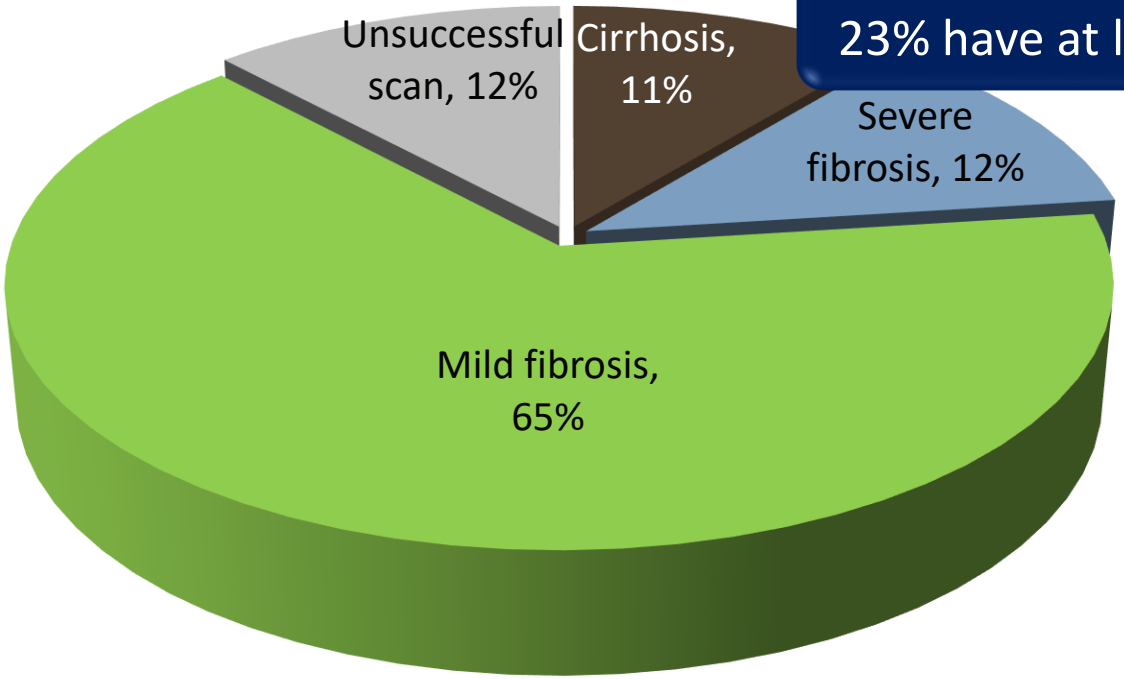
1. HCV Antibody test
   - Exposure to virus, remains positive after virus cleared
2. HCV RNA
   - Indicates current infection
3. HCV Genotype
   - Determines eligibility for treatment with funded drugs.
   - Check if last genotype result >5 years ago

Testing for HCV: only request the **HCV Antibody test.** LabPLUS will do reflex HCV RNA and genotyping for you.

Why we need to treat HepC

Ageing population with increasing disease severity

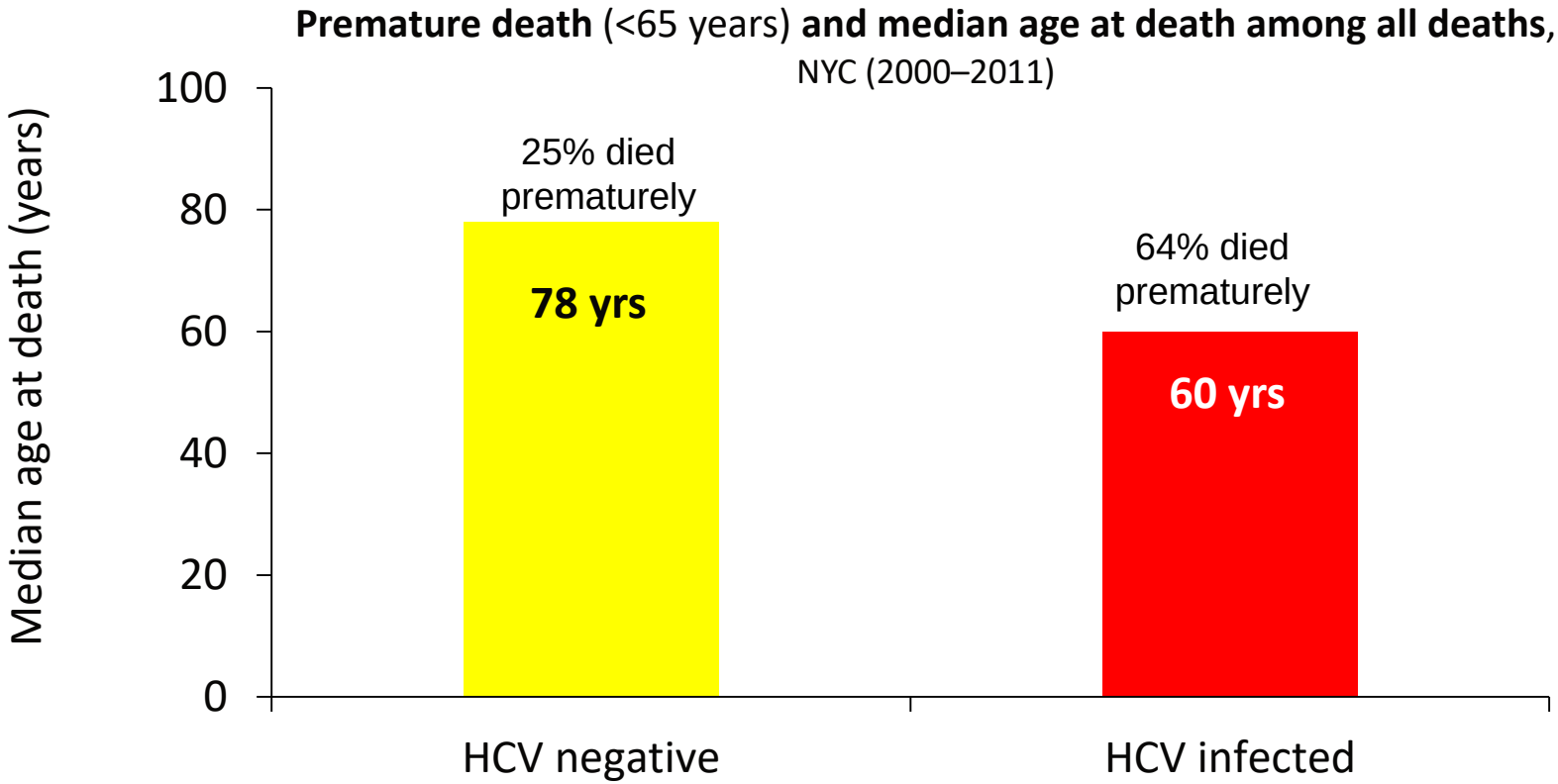
Ministry of Health HCV Pilot in Bay of Plenty and Wellington:
788 Fibroscans in newly diagnosed patients



11% have established cirrhosis
23% have at least severe fibrosis

Hepatitis Foundation of NZ. Report; Nov 2014.

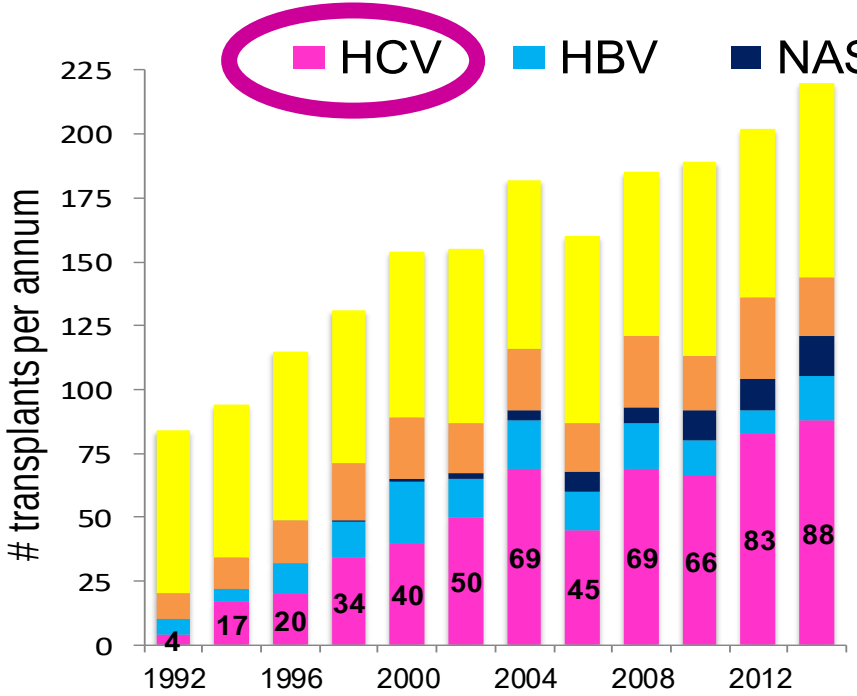
Falling life expectancy from chronic hepatitis C



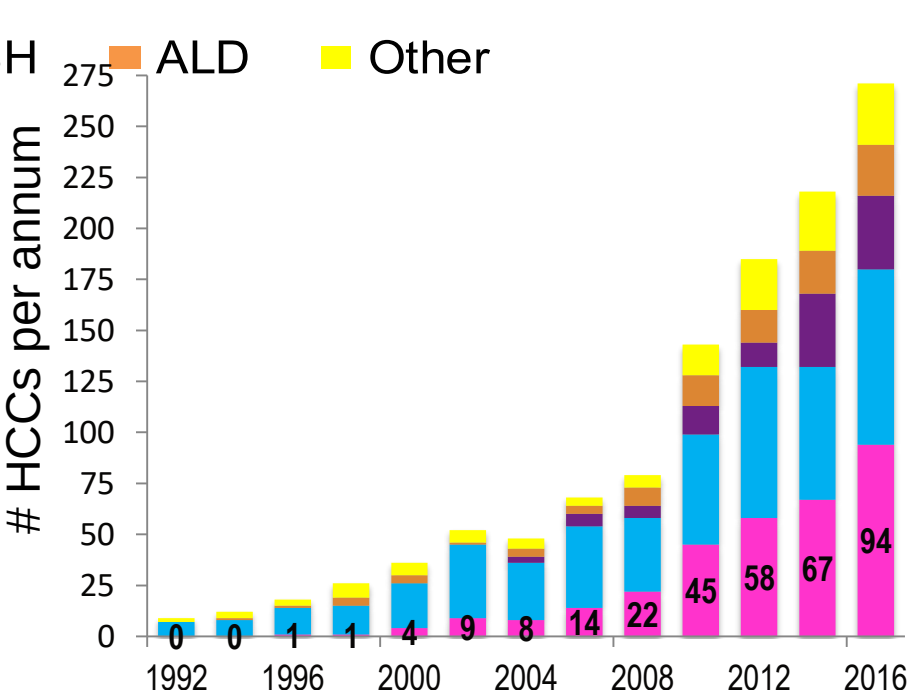
Pinchoff J, et al. Clin Infect Dis 2014;58:1047–54.

Increasing disease burden from chronic hepatitis C

Liver Transplants (ANZLTR)

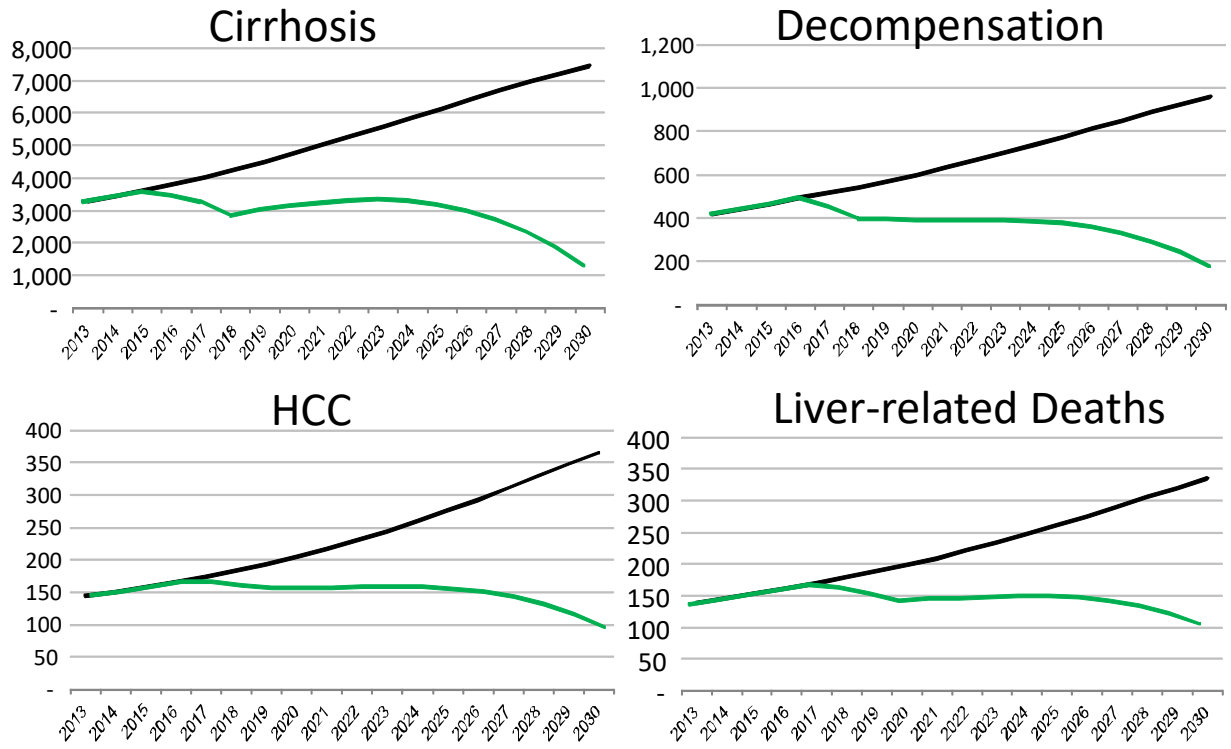


Liver Cancer (NZLTU)



26th Australian and New Zealand Liver Transplant Registry. http://www.slhd.nsw.gov.au/gastro/livertransplant/pdf/ANZLTR_26th_Report.pdf Accessed July 2015.

And it is going to get worse, unless……



Interferon
→ 1% treated
→50% cure rate

New oral DAAs
→ 10% treated
→ 90% cure rate

Gane E, et al. *NZ Med J* 2014;127(1407):61–74.

What will it take to eliminate HCV from NZ?

Identify the 20,000 patients who remain undiagnosed

- Target testing in primary care, including point-of-care testing in Prisons, Needle Exchanges, Community Alcohol and Drug Services.

Improve access to safe and effective treatments

- Continue to treat and follow-up sickest patients in secondary care.
- Offer assessment and treatment for most patients in primary care.

Prevent transmission and reinfection

- Broaden access to sterile equipment for high-risk activities, and provide education and support to reduce risk factors.

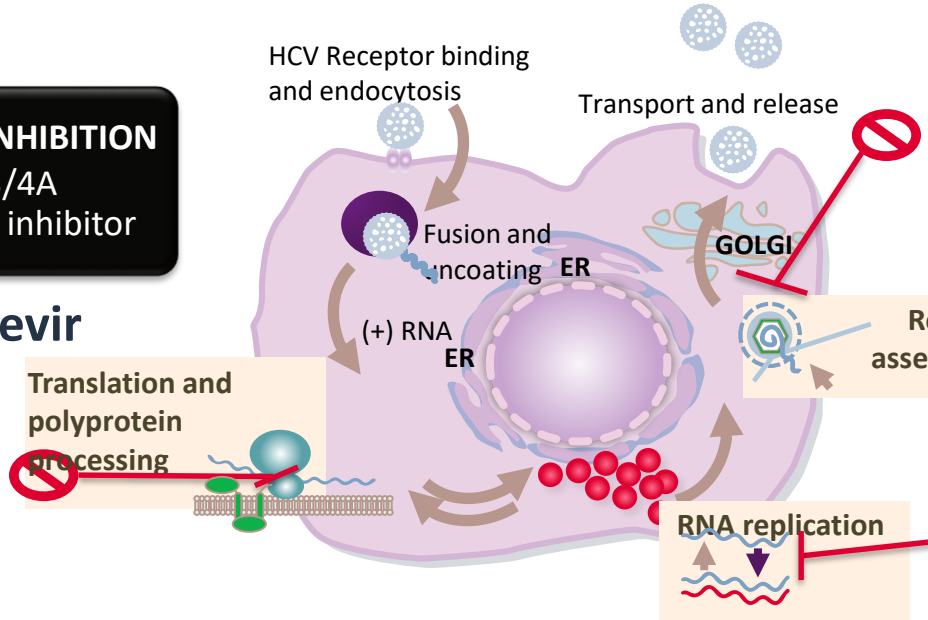
Gane E, et al. *NZ Med J* 2014;127(1407):61–74.

VIEKIRA PAK (ombitasvir/paritaprevir/ritonavir with dasabuvir)

Mode of Action

1. EARLY INHIBITION
NS3/4A
protease inhibitor

Paritaprevir
(PTV)



3. MID-/LATE LIFECYCLE INHIBITION
NS5A inhibitor

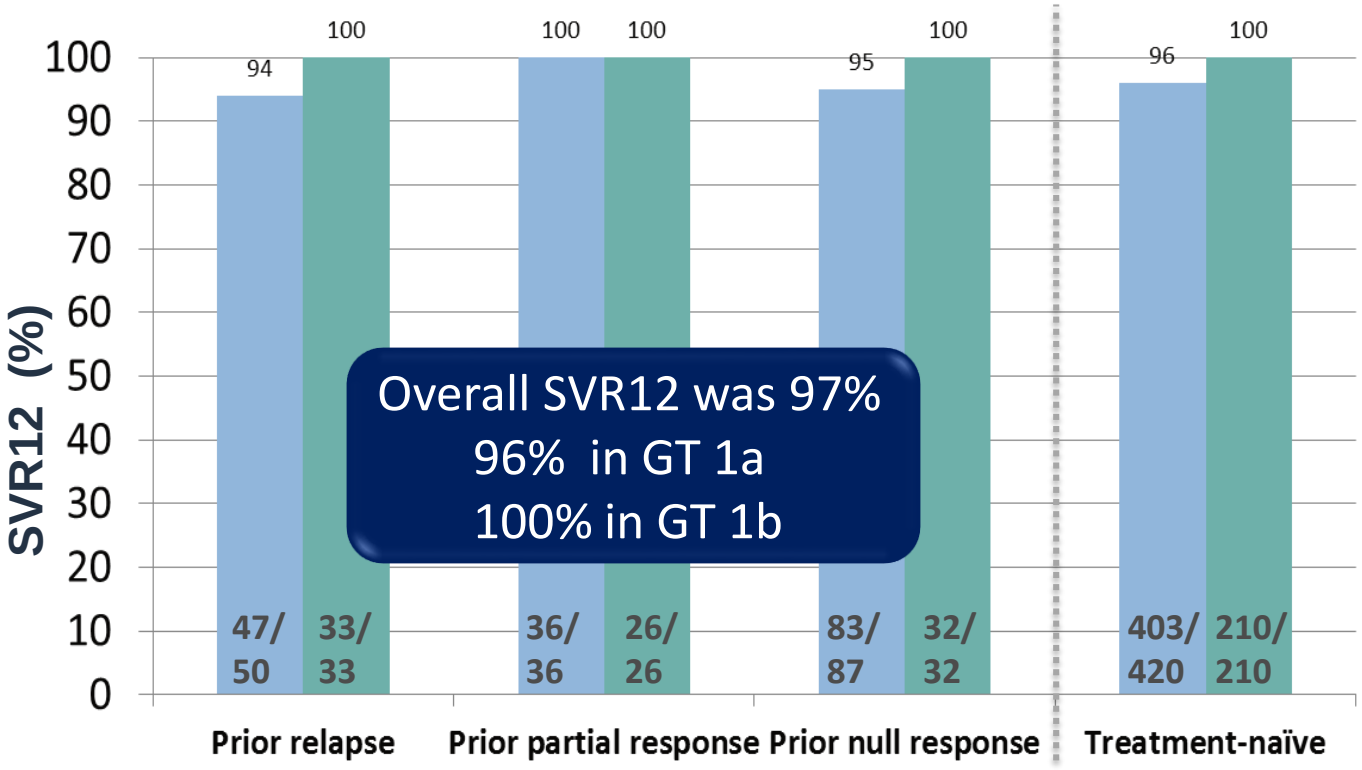
Ombitasvir
(OBV)

2. MID-LIFECYCLE INHIBITION
non-nucleoside
NS5B polymerase inhibitor

Dasabuvir
(DSV)

Lindenbach & Rice. Nature 2005;436:933–38.
AbbVie Limited. VIEKIRA PAK and VIEKIRA PAK-RBV Data Sheets. Medsafe New Zealand; version 10: May 2017.

VIEKIRA PAK in HCV genotype 1 patients without cirrhosis

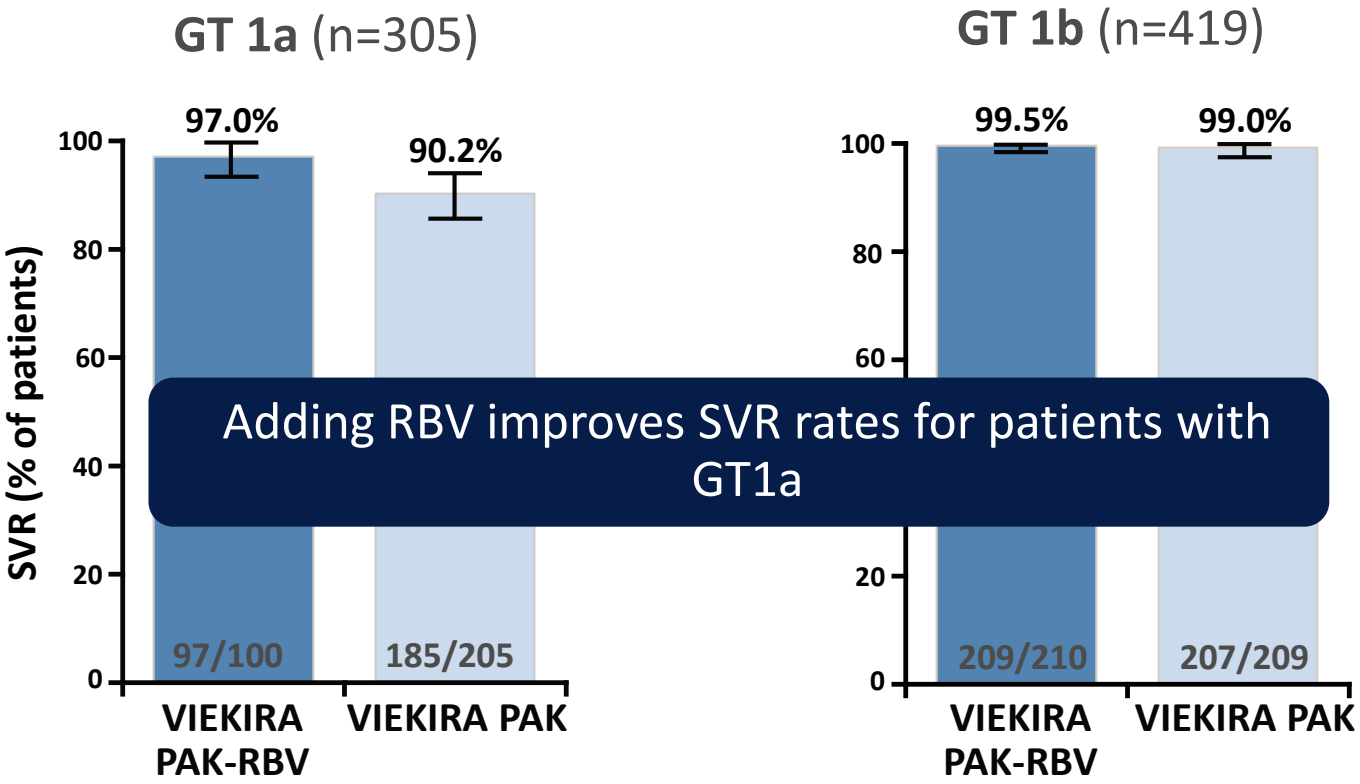


- 1025 GT 1 patients received VIEKIRA PAK-RBV for 12 weeks
- 394 had already failed interferon treatment

GT1a
GT1b

Feld J, et al. *N Engl J Med* 2014;370:1594-603. Zeuzem S, et al. *N Engl J Med* 2014;370:1604-14.

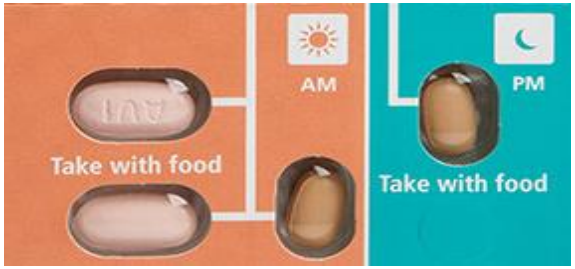
Patients with HCV GT 1a need addition of ribavirin



Ferenci P, et al. N Eng J Med 2014;370:1983–92.

Constituents of VIEKIRA PAK for HCV GT 1b

Co-formulated paritaprevir/ritonavir (PTV/r) 75 mg/50 mg plus ombitasvir (OBV) 12.5 mg tablets



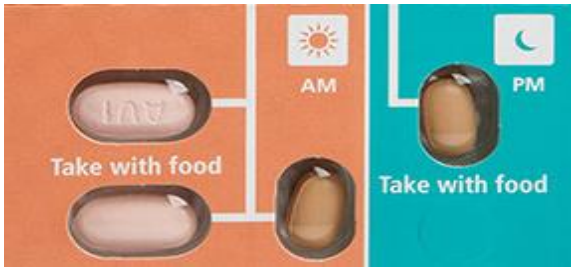
Dasabuvir (DSV) 250 mg tablets

VIEKIRA PAK is taken with food, as three tablets in the morning and one in the evening.

AbbVie Limited. VIEKIRA PAK and VIEKIRA PAK-RBV Data Sheets. Medsafe New Zealand; version 10: May 2017.

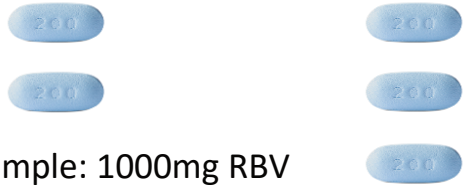
Constituents of VIEKIRA PAK-RBV for HCV GT 1a

Co-formulated paritaprevir/ritonavir (PTV/r) 75 mg/50 mg plus ombitasvir (OBV) 12.5 mg tablets



Dasabuvir (DSV) 250 mg tablets

Ribavirin, weight-based dose, 200 mg tablets



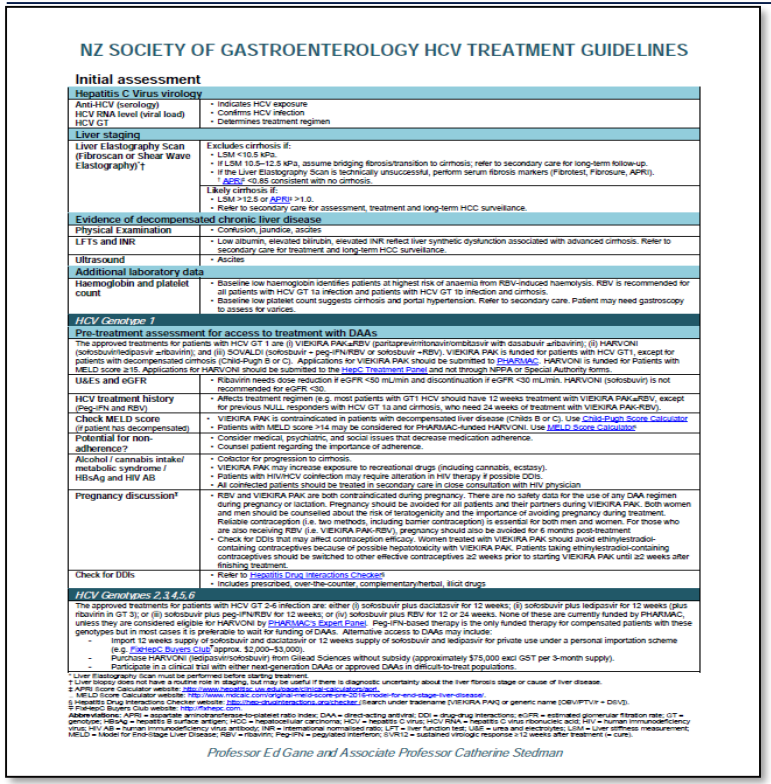
Example: 1000mg RBV dose for a patient ≤ 75kg

- Ribavirin is a synthetic nucleoside analogue with HCV antiviral activity.
- Most patients should start on 1000 or 1200 mg, depending on bodyweight.
- Patients with renal dysfunction or vascular disease start with a lower dose.

AbbVie Limited. VIEKIRA PAK and VIEKIRA PAK-RBV Data Sheets. Medsafe New Zealand; version 10: May 2017.

Treatments for hepatitis C:
prescribing and monitoring guidelines

NZSG HCV Treatment Guidelines, endorsed by ASID, RNZCGPS



NZ SOCIETY OF GASTROENTEROLOGY HCV TREATMENT GUIDELINES

Initial assessment

Hepatitis C Virus virology	
Anti-HCV (serology) HCV RNA level (viral load) HCV GT	• Indicates HCV exposure • Confirms HCV infection • Determines treatment regimen
Liver staging	
Liver Elastography Scan (Fibroscan or Shear Wave Elastography)*†	Excludes cirrhosis if: • LSM <10.5 kPa. • If LSM 10.5–12.5 kPa, assume bridging fibrosis/transition to cirrhosis; refer to secondary care for long-term follow-up. • If the Liver Elastography Scan is technically unsuccessful, perform serum fibrosis markers (Fibrotest, Fibrosure, APRI). * APRI‡ <0.85 consistent with no cirrhosis.
	Likely cirrhosis if: • LSM >12.5 or APRI‡ >1.0. • Refer to secondary care for assessment, treatment and long-term HCC surveillance.
Evidence of decompensated chronic liver disease	
Physical Examination	• Confusion, jaundice, ascites
LFTs and INR	• Low albumin, elevated bilirubin, elevated INR reflect liver synthetic dysfunction associated with advanced cirrhosis. Refer to secondary care for treatment and long-term HCC surveillance.
Ultrasound	• Ascites
Additional laboratory data	
Haemoglobin and platelet count	• Baseline low haemoglobin identifies patients at highest risk of anaemia from RBV-induced haemolysis. RBV is recommended for all patients with HCV GT 1a infection and patients with HCV GT 1b infection and cirrhosis. • Baseline low platelet count suggests cirrhosis and portal hypertension. Refer to secondary care. Patient may need gastroscopy to assess for varices.
HCV Genotype 1	
Pre-treatment assessment for access to treatment with DAAs	
The approved treatments for patients with HCV GT 1 are (i) VIEKIRA PAK+RBV (paritaprevir/ritonavir/ombitasvir with dasabuvir ±ribavirin); (ii) HARVONI (sofosbuvir/ledipasvir ±ribavirin); and (iii) SOVALDI (sofosbuvir + peg-IFN/RBV or sofosbuvir +RBV). VIEKIRA PAK is funded for patients with HCV GT1, except for patients with decompensated cirrhosis (Child-Pugh B or C). Applications for VIEKIRA PAK should be submitted to PHARMAC. HARVONI is funded for Patients with MELD score ≥15. Applications for HARVONI should be submitted to the HepC Treatment Panel and not through NPPA or Special Authority forms.	
UAEs and eGFR	• Ribavirin needs dose reduction if eGFR <50 mL/min and discontinuation if eGFR <30 mL/min. HARVONI (sofosbuvir) is not recommended for eGFR <30.
HCV treatment history (Peg-IFN and RBV)	• Affects treatment regimen (e.g. most patients with GT1 HCV should have 12 weeks treatment with VIEKIRA PAK+RBV, except for previous Null responders with HCV GT 1a and cirrhosis, who need 24 weeks of treatment with VIEKIRA PAK+RBV).
Check MELD score (if patient has decompensated)	• VIEKIRA PAK is contraindicated in patients with decompensated liver disease (Childs B or C). Use Child-Pugh Score Calculator • Patients with MELD score >14 may be considered for PHARMAC-funded HARVONI. Use MELD Score Calculator§
Potential for non-adherence?	• Consider medical, psychiatric, and social issues that decrease medication adherence. • Counsel patient regarding the importance of adherence.
Alcohol / cannabis intake/ metabolic syndrome / HBsAg and HIV Ab	• Cofactor for progression to cirrhosis. • VIEKIRA PAK may increase exposure to recreational drugs (including cannabis, ecstasy). • Patients with HIV/HCV coinfection may require alteration in HIV therapy if possible DDIs. • All coinfected patients should be treated in secondary care in close consultation with HIV physician
Pregnancy discussion¶	• RBV and VIEKIRA PAK are both contraindicated during pregnancy. There are no safety data for the use of any DAA regimen during pregnancy or lactation. Pregnancy should be avoided for all patients and their partners during VIEKIRA PAK. Both women and men should be counselled about the risk of teratogenicity and the importance of avoiding pregnancy during treatment. Reliable contraception (i.e. two methods, including barrier contraception) is essential for both men and women. For those who are also receiving RBV (i.e. VIEKIRA PAK-RBV), pregnancy should also be avoided for 6 months post-treatment. • Check for DDIs that may affect contraception efficacy. Women treated with VIEKIRA PAK should avoid ethinylestradiol-containing contraceptives because of possible hepatotoxicity with VIEKIRA PAK. Patients taking ethinylestradiol-containing contraceptives should be switched to other effective contraceptives ≥2 weeks prior to starting VIEKIRA PAK until ≥2 weeks after finishing treatment.
Check for DDIs	• Refer to Hepatitis Drug Interactions Checker¶ • Includes prescribed, over-the-counter, complementary/herbal, illicit drugs
HCV Genotypes 2,3,4,5,6	
The approved treatments for patients with HCV GT 2-6 infection are: either (i) sofosbuvir plus daclatasvir for 12 weeks; (ii) sofosbuvir plus ledipasvir for 12 weeks (plus ribavirin in GT 3); or (iii) sofosbuvir plus peg-IFN/RBV for 12 weeks; or (iv) sofosbuvir plus RBV for 12 or 24 weeks. None of these are currently funded by PHARMAC, unless they are considered eligible for HARVONI by PHARMAC's Expert Panel. Peg-IFN-based therapy is the only funded therapy for compensated patients with these genotypes but in most cases it is preferable to wait for funding of DAAs. Alternative access to DAAs may include: - Import 12 weeks supply of sofosbuvir and daclatasvir or 12 weeks supply of sofosbuvir and ledipasvir for private use under a personal importation scheme (e.g. FlatHepC Buyers Club) approx. $2,000–$3,000). - Purchase HARVONI (ledipasvir/sofosbuvir) from Gilead Sciences without subsidy (approximately $75,000 excl GST per 3-month supply). - Participate in a clinical trial with either next-generation DAAs or approved DAAs in difficult-to-treat populations.	

* Liver Elastography scan must be performed before starting treatment.
† Liver biopsy does not have a routine role in staging, but may be useful if there is diagnostic uncertainty about the liver fibrosis stage or cause of liver disease.
‡ APRI Score Calculator website: http://www.hepatitis.va.gov/hcv/assessment/clinical-calculators.asp#.
§ MELD Score Calculator website: http://www.mdcalc.com/original-meld-score-pre-2016-model-for-end-stage-liver-disease/.
¶ Hepatitis Drug Interactions Checker website: http://hep-druginteractions.org/checker (Search under tradename [VIEKIRA PAK] or generic name [OBV/PTV/r + DSV]).
# FlatHepC Buyers Club website: http://flathepc.com.

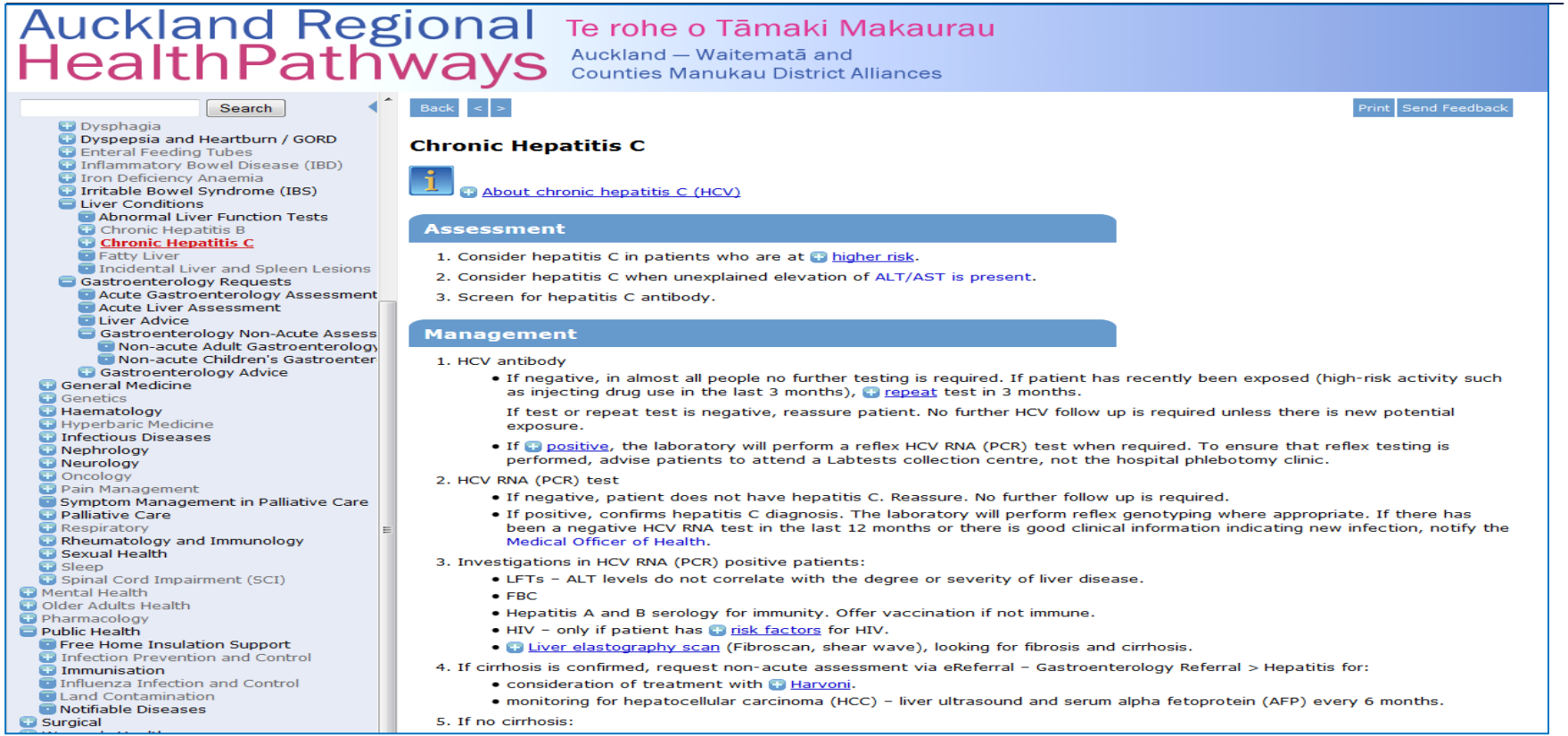
Abbreviations: APRI = aspartate aminotransferase-to-platelet ratio index; DAA = direct-acting antiviral; DDI = drug-drug interactions; eGFR = estimated glomerular filtration rate; GT = genotype; HBsAg = hepatitis B surface antigen; HCC = hepatocellular carcinoma; HCV = hepatitis C virus; HCV RNA = hepatitis C virus ribonucleic acid; HIV = human immunodeficiency virus; HIV Ab = human immunodeficiency virus antibody; INR = international normalized ratio; LFT = liver function test; UAE = urea and electrolytes; LSM = Liver stiffness measurement; MELD = Model for End-Stage Liver Disease; RBV = ribavirin; Peg-IFN = pegylated interferon; SVR12 = sustained virologic response ≥12 weeks after treatment (= cure).

Professor Ed Gane and Associate Professor Catherine Stedman

Available at:
http://www.nzsg.org.nz/cms2/guidelines/

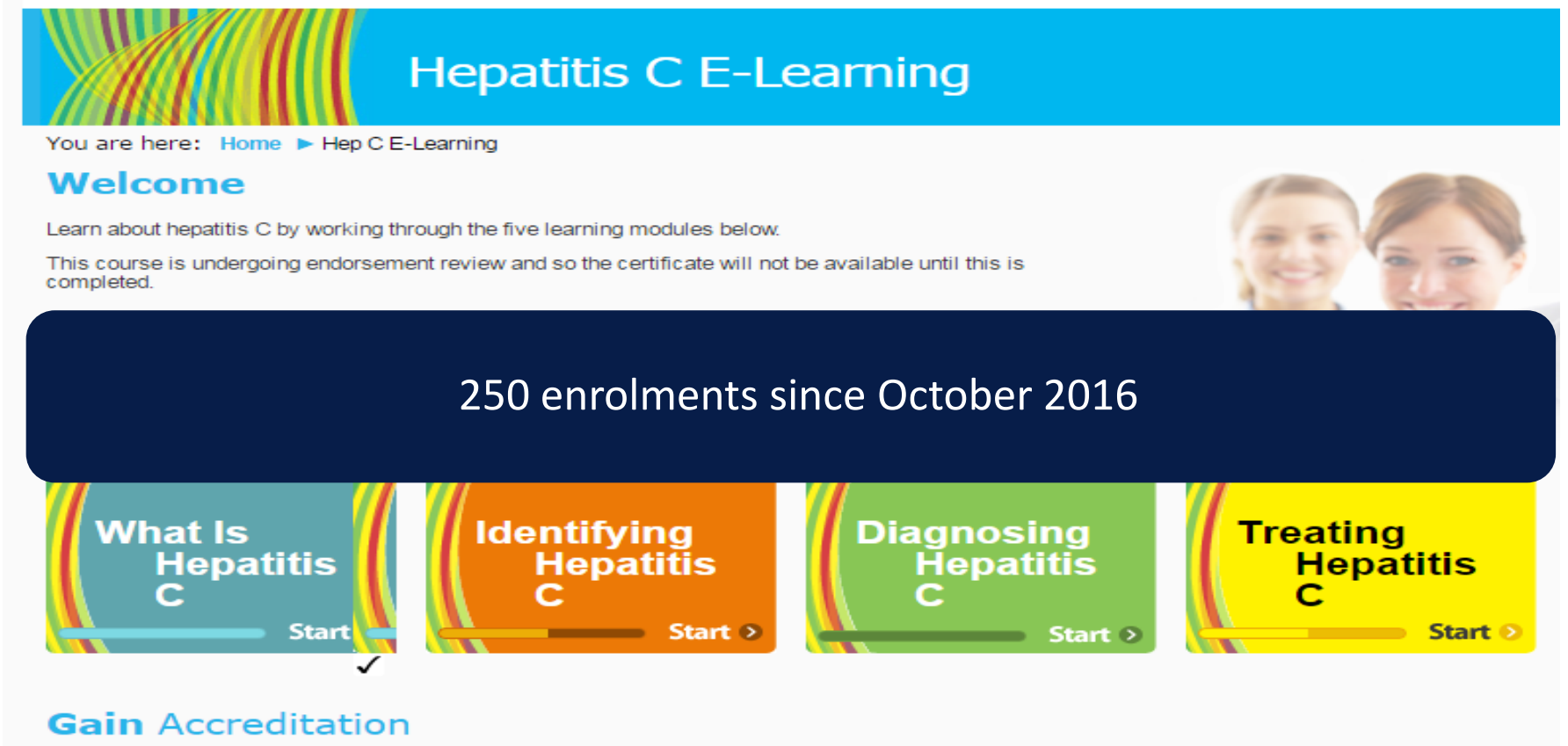
Gane, Stedman. NZ Society of Gastroenterology HCV Treatment Guidelines. 2016. Available at: http://www.nzsg.org.nz/cms2/uploads/2017/NZSG%20Hepatitis%20C%20Guidance_November%20UPDATE.pdf

Auckland Regional Health Pathways



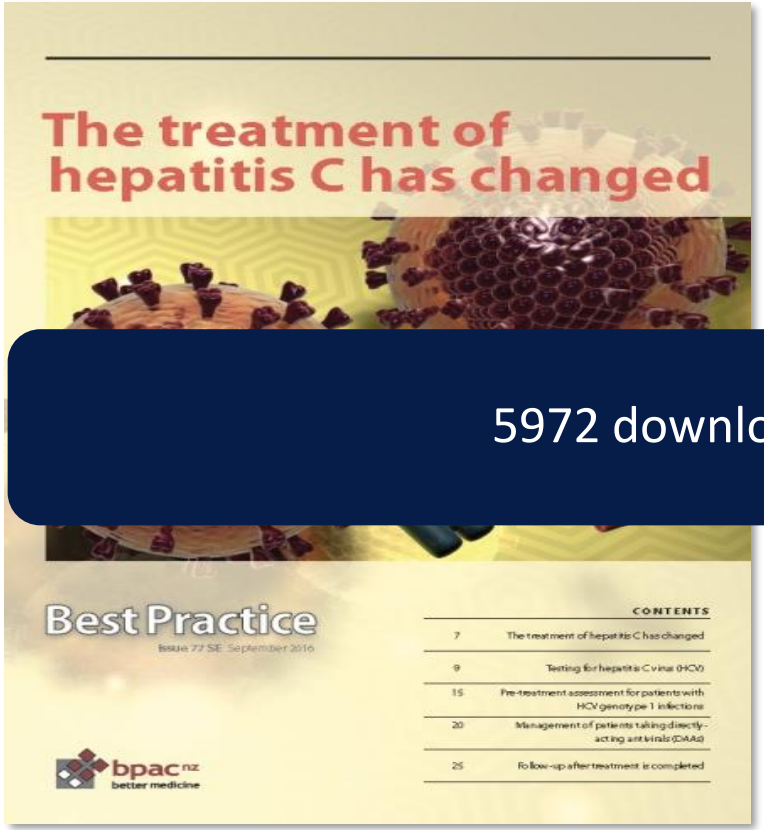
Auckland Regional Health Pathways. Available at: http://aucklandregion.healthpathways.org.nz/index.htm

Ministry of Health e-learning



Ministry of Health e-learning. Available at: http://learnonline.health.nz/course/category.php?id=9

Ministry of Health /BPAC

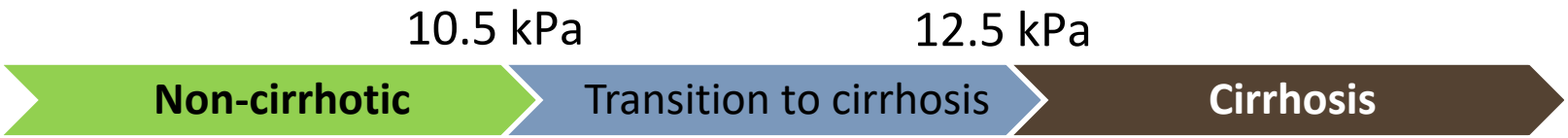


Available at:
http://www.bpac.org.nz/2016/hepc

5972 downloads since October 2016

Pre-treatment assessment for VIEKIRA PAK: liver

Tests	Rationale
Non-invasive liver staging	Patients with liver stiffness measurement (LSM) >10.5 kPa on Fibroscan or shearwave elastography: ***refer to secondary care***
Blood count	Low **platelet count** (<100 cells x10^9L) suggests portal hypertension and risk of AEs: ***refer to secondary care***
Liver function tests	Low albumin (<35 g/L) suggests cirrhosis***: refer to secondary care.***



All patients with cirrhosis, or in transition to cirrhosis, should be referred to secondary care for treatment and follow-up.

Gane, Stedman. NZSG Treatment Guidelines. 2016. Available at http://www.nzsg.org.nz/cms2/guidelines/ Accessed December 2016.
AbbVie Limited. VIEKIRA PAK and VIEKIRA PAK-RBV Data Sheets. Medsafe New Zealand; version 10: May 2017.

Top of Form

ADHB Hepatitis Referral for Outpatient Appointment

Patient: Donald J Duck, 62yrs, **NHI AAA1111**, M, DOB 01/01/1951, PH: Wrk 022 000 4444, Hme 888 11111
Residential address: 22 Disney Lane, Annaheim, Auckland 01111
Postal address: same as residential address
Referred by: Graham Gulbransen, Kingsland Family Health Centre, NZMC 11258, PH 815 1475, FAX 846 7195
Referral date: 03/05/2017 11:28 NZST

Clinical Referral Information

GASTROENTEROLOGY - HEPATITIS
Reason for referral:
Fibroscan
Referral details:
Date: 03/05/2017 11:27:01 would like hep C treatment
no needle use
considering VIEKIRA PAK
Poor venous access
Measurement Details

Date	Code	Value
30/09/2015	Height	174
30/09/2015	Weight	70.6
Date	**Code**	**Value**
30/09/2015	BMI	23.3

Diagnostic Reports / Patient Documents

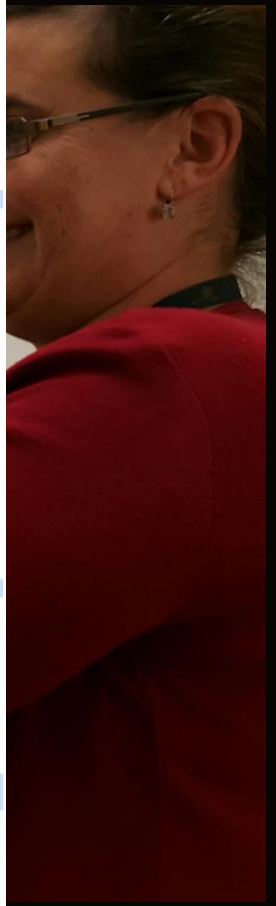
Date	Name	Comments	Size
19/12	Hcv Genotyping	GT 1a gg	1 KB
19/12	Alpha Fetoprotein	3.2 gg	1 KB
19/12	Hep C Viral Load	pos gg	1 KB
19/12	DiabeticProfile	33 gg	1 KB
19/12	Complete Blood Count	Hb 108 hcv gg	2 KB
19/12	LiverFunctionTests	ggt 116 gg	1 KB

File Attachments - No files attached

Diagnostic Reports / Patient Documents - Hcv Genotyping

Patient Details
Patient Name: Duck, Donald
NHI No:
Date of Birth: 01-Jan-1954

HCV Genotyping Result: 1a
Please note this assay has been recently updated and is now performed on a different platform. Please refer to the
LabPlus test guide for new detection limits and assay details.



Can cirrhosis status be determined without a Fibroscan?

1. Previous biopsy (within 5 years)

2. Serum test: AST to Platelet Ratio Index (APRI)
   <1.0 = no cirrhosis ⇨ treat in General Practice
   ≥1.0 = possible cirrhosis ⇨ refer to Secondary Care
   Use the free online calculator: https://www.mdcalc.com/ast-platelet-ratio-index-apri

Pre-treatment assessment: Contraindications

Contraindications for VIEKIRA PAK

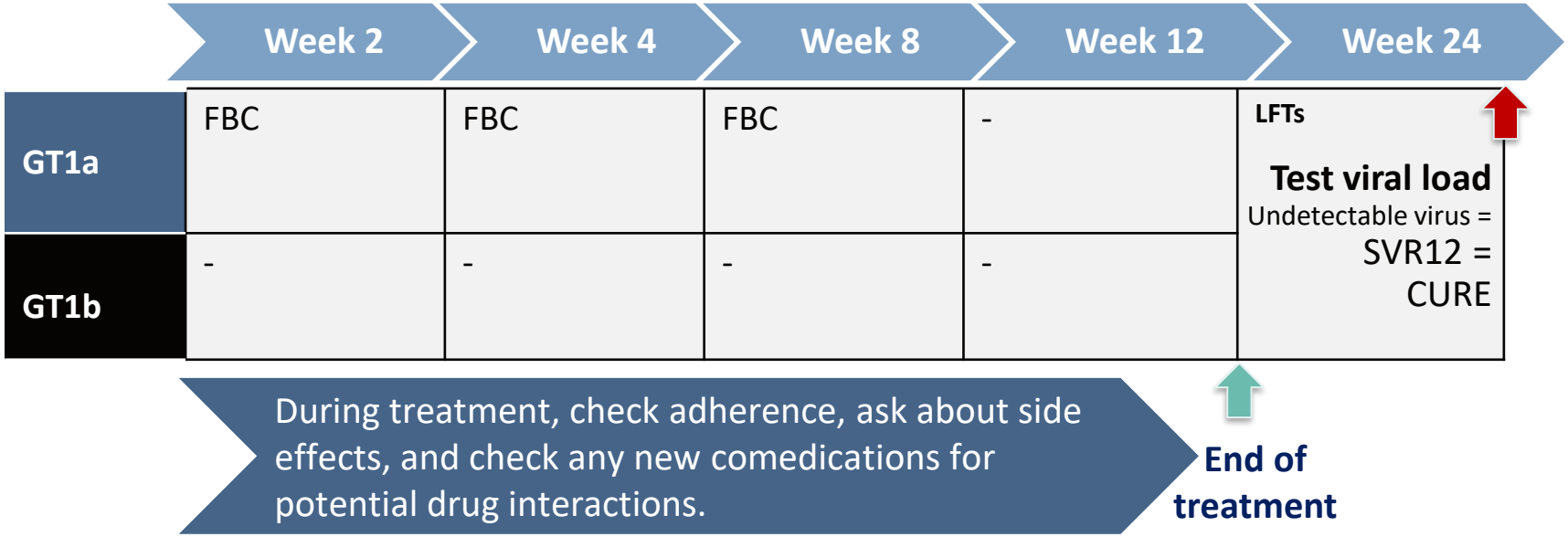
- **Severe hepatic impairment** (Child-Pugh C).
- **Co-administration with drugs** that are highly dependent on CYP3A for clearance, are moderate or strong inducers of CYP3A, or are strong inducers or inhibitors of CYP2C8.

Contraindications for Ribavirin (in HCV GT 1a)

- **Pregnancy** (including of a partner).
- History of **severe, unstable, or uncontrolled cardiac disease** in past 6 months.
- **Haemoglobinopathies** (e.g. thalassaemia).

AbbVie Limited. VIEKIRA PAK and VIEKIRA PAK-RBV Data Sheets. Medsafe New Zealand; version 10: May 2017.

VIEKIRA PAK-RBV: safety monitoring during treatment



FBC – full blood count.

VIEKIRA PAK and VIEKIRA PAK-RBV Data Sheets. Medsafe New Zealand; version 10: May 2017.
Gane, Stedman. NZ Society of Gastroenterology HCV Treatment Guidelines. 2016. http://www.nzsg.org.nz/cms2/guidelines/

Likelihood of common side effects

VIEKIRA PAK

Fatigue (tiredness)		20-30%
Insomnia (trouble sleeping), itchy skin or nausea		5-10%

VIEKIRA PAK-RBV

Fatigue (tiredness)		30-40%
Nausea		20-30%
Insomnia (trouble sleeping), itchy skin or weakness		10-20%
Anaemia		5-10%
Decreased appetite, dizziness, diarrhoea, dry skin, headaches, rash or vomiting		Less than 5%

Based on adverse events that occurred 5% more often with VIEKIRA PAK and VIEKIRA PAK-RBV than with placebo.

VIEKIRA PAK and VIEKIRA PAK-RBV Data Sheets. Medsafe New Zealand; version 10: May 2017.

Management of side effects

Fatigue/ anaemia: Check haemoglobin level and adjust ribavirin dosage according to Data Sheet and Guidelines.

Nausea: Consider ondansetron at the standard recommended dosage.

Insomnia: Consider advice on improved sleep hygiene. If severe, consider using temazepam 10 mg or zopiclone 3.75 mg when required.

Skin rash: Use 10% urea cream, Pinetarsol, or fatty cream. Consult DermNet NZ.

Management of common comorbidities

Depression: Citalopram or escitalopram are allowed.

Gane, Stedman. NZ Society of Gastroenterology HCV Treatment Guidelines. 2016. http://www.nzsg.org.nz/cms2/guidelines/ Accessed December 2016.

AbbVie reporting of adverse events

An adverse event is **any** untoward medical occurrence in a patient given a medicinal product, including death, hospitalisation, surgery, or any worsening of a patient's condition; overdose, abuse, or misuse; inadvertent, accidental, or occupational exposure; use during pregnancy or breastfeeding; lack of effect; medication error; suspected transmission of an infectious agent via a medicinal product; off-label use with an adverse event; and unexpected benefit.

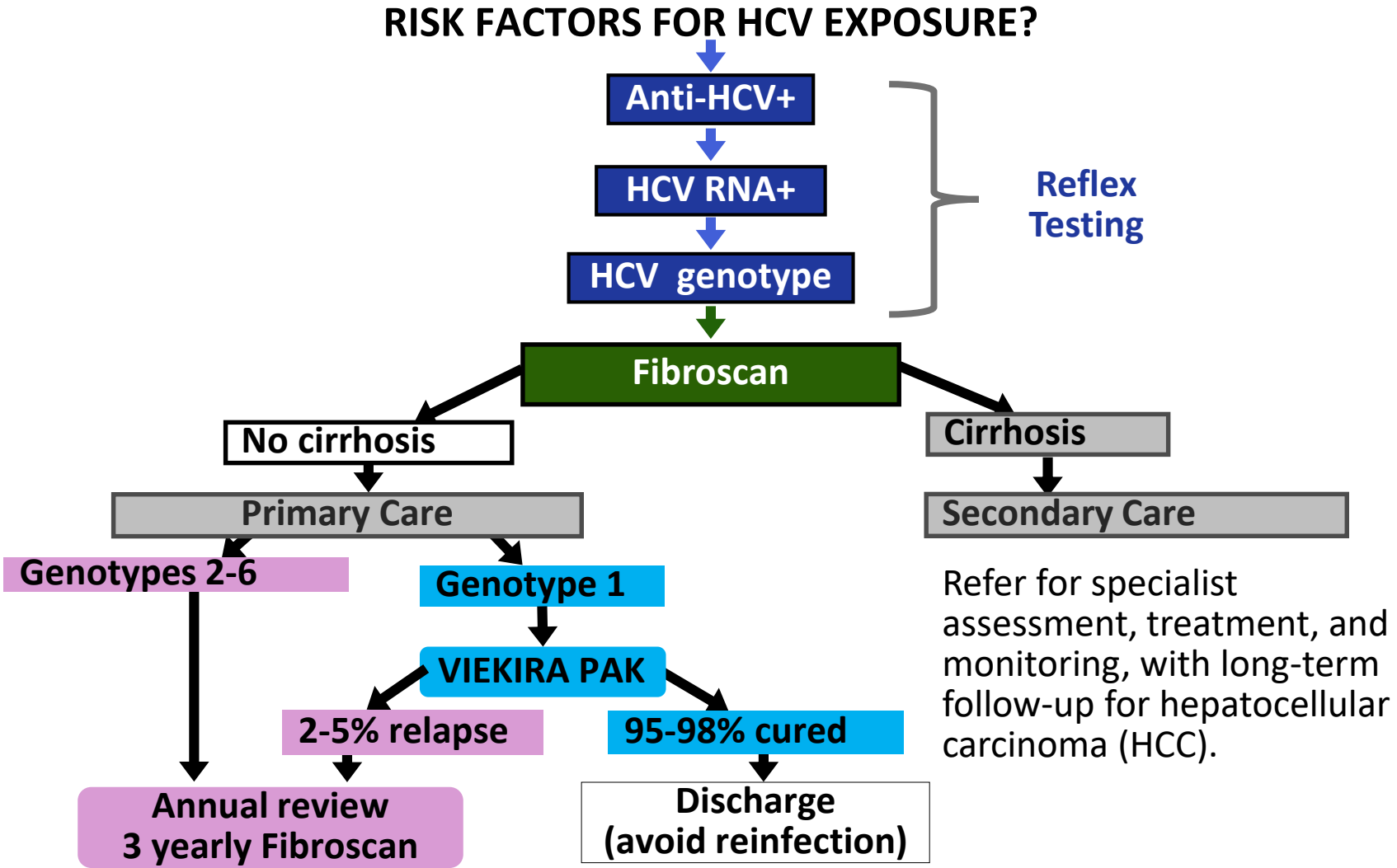
Please report any adverse event regarding VIEKIRA PAK or VIEKIRA PAK-RBV:

- email: anzpv@abbvie.com or phone: 0800 900 030

or

- email NZ's National Centre for Adverse Reactions Monitoring (CARM): carmnz@otago.ac.nz

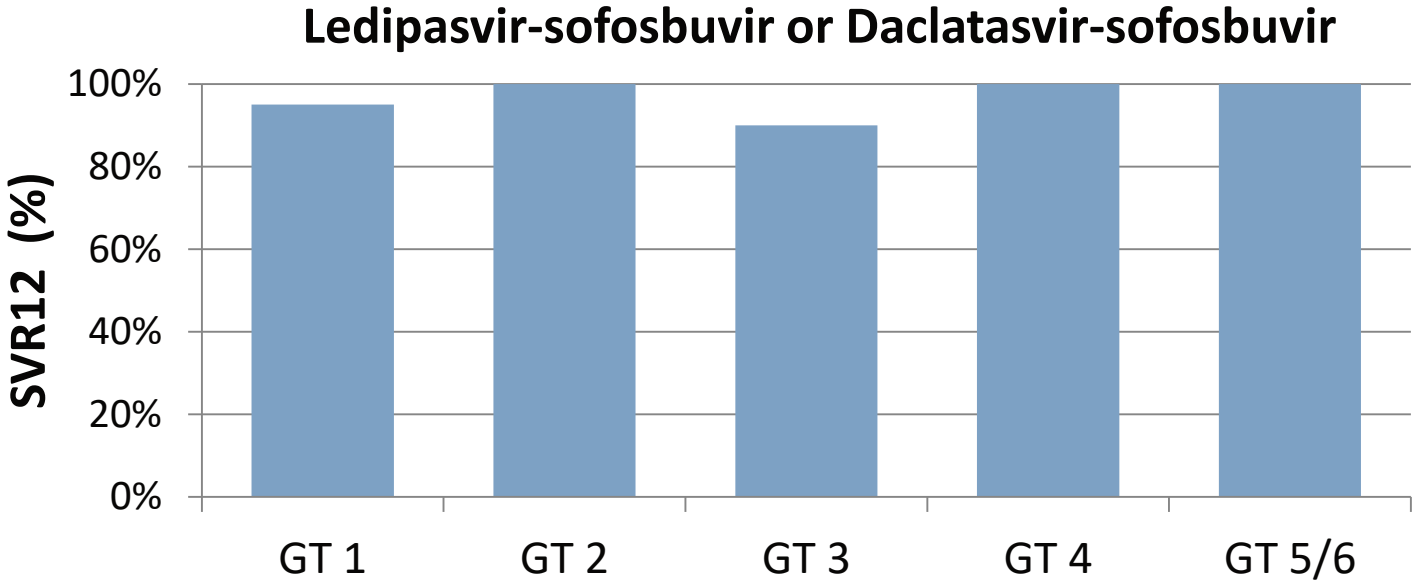
All such reports are added to the appropriate national and global safety databases to enable monitoring of aggregated data.


RISK FACTORS FOR HCV EXPOSURE?
Anti-HCV+
HCV RNA+
HCV genotype
Reflex Testing
Fibroscan
No cirrhosis
Cirrhosis
Primary Care
Secondary Care
Genotypes 2-6
Genotype 1
VIEKIRA PAK
2-5% relapse
95-98% cured
Annual review
3 yearly Fibroscan
Discharge
(avoid reinfection)
Refer for specialist assessment, treatment, and monitoring, with long-term follow-up for hepatocellular carcinoma (HCC).

What about patients with HCV GT 2–6?

Importing 12 weeks of DAAs is permitted by Medsafe (prescription, Customs declaration, $2000–2500).

Efficacy and safety similar to clinical trials.



Treatments for hepatitis C:
Management of drug interactions

VIEKIRA PAK: Drug–drug interactions

- All DAAs interact with drug metabolising enzymes or transporters.
- Ribavirin is associated with additional drug interactions.
- Drug interactions could reduce clinical efficacy or cause adverse events.
- **All patients need a careful medicines review before treatment.**
- Most potential drug interactions can be managed by adjustment of dose and/or monitoring during treatment for any potential adverse reactions. No dose adjustment is needed for VIEKIRA PAK itself.
- Some medications are contraindicated, and must be stopped, or substituted with alternatives, during treatment.

AbbVie Limited. VIEKIRA PAK and VIEKIRA PAK-RBV Data Sheets. Medsafe New Zealand; version 10: May 2017. University of Liverpool website: http://hep-druginteractions.org/. Gane, Stedman. NZSG Treatment Guidelines. 2016. Available at http://www.nzsg.org.nz/cms2/uploads/2017/NZSG%20Hepatitis%20C%20Guidance_November%20UPDATE.pdf

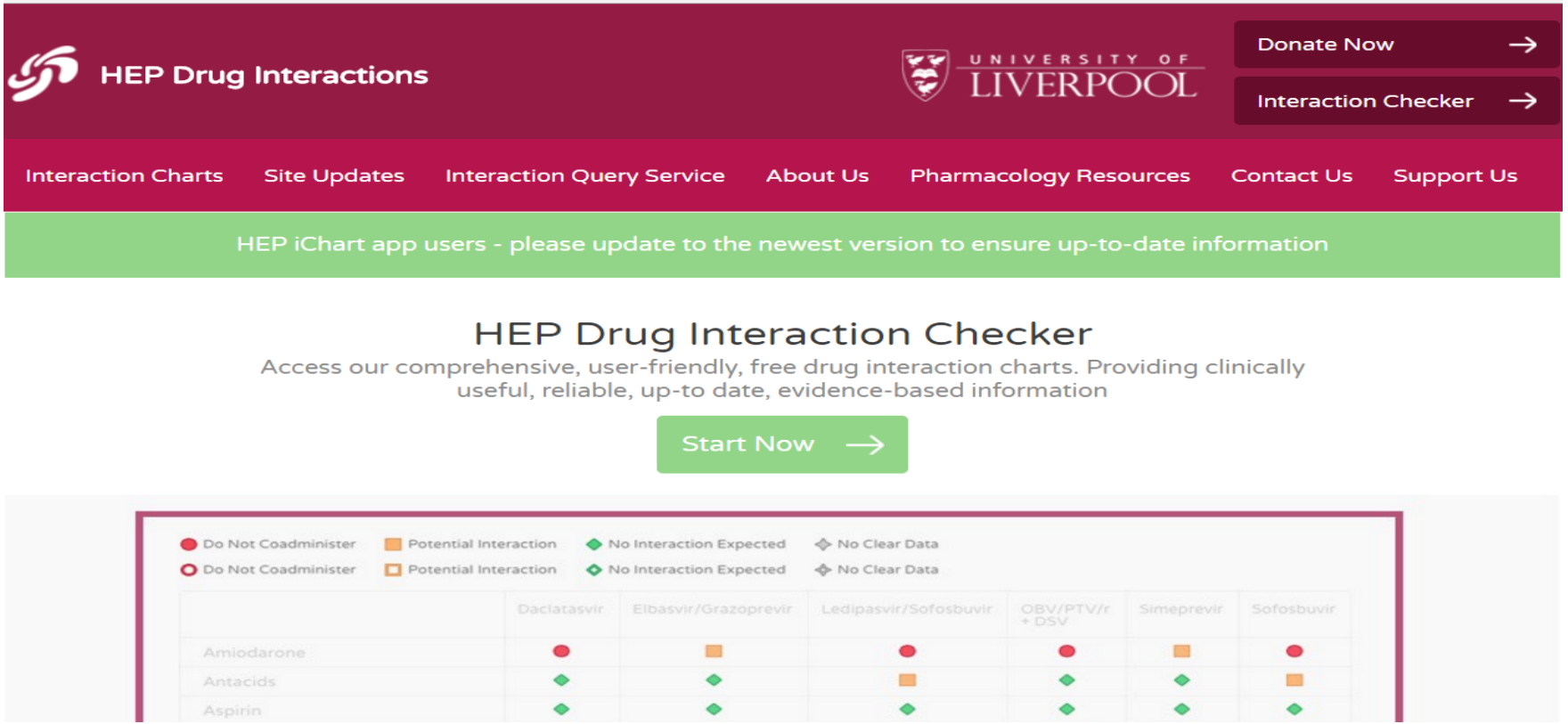
Where to find information on interactions

1. **Medsafe-approved Data Sheets**: 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 or by drug class.

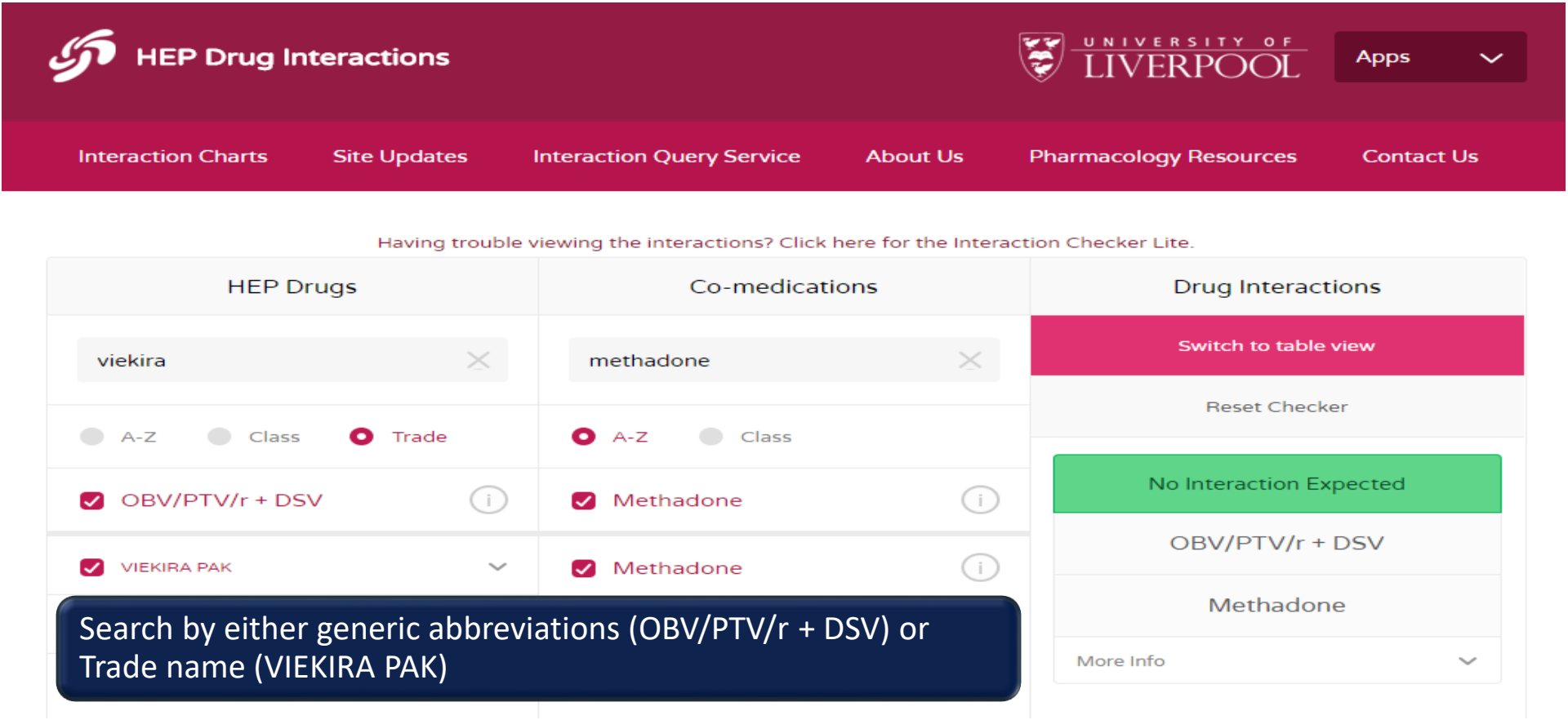
3. **AbbVie Medical Information:** 0800 900 030, medinfoanz@abbvie.com
   AbbVie can answer questions based on 'Data on File', built up through the clinical development programme and post-marketing experience.

Online resource: University of Liverpool's website

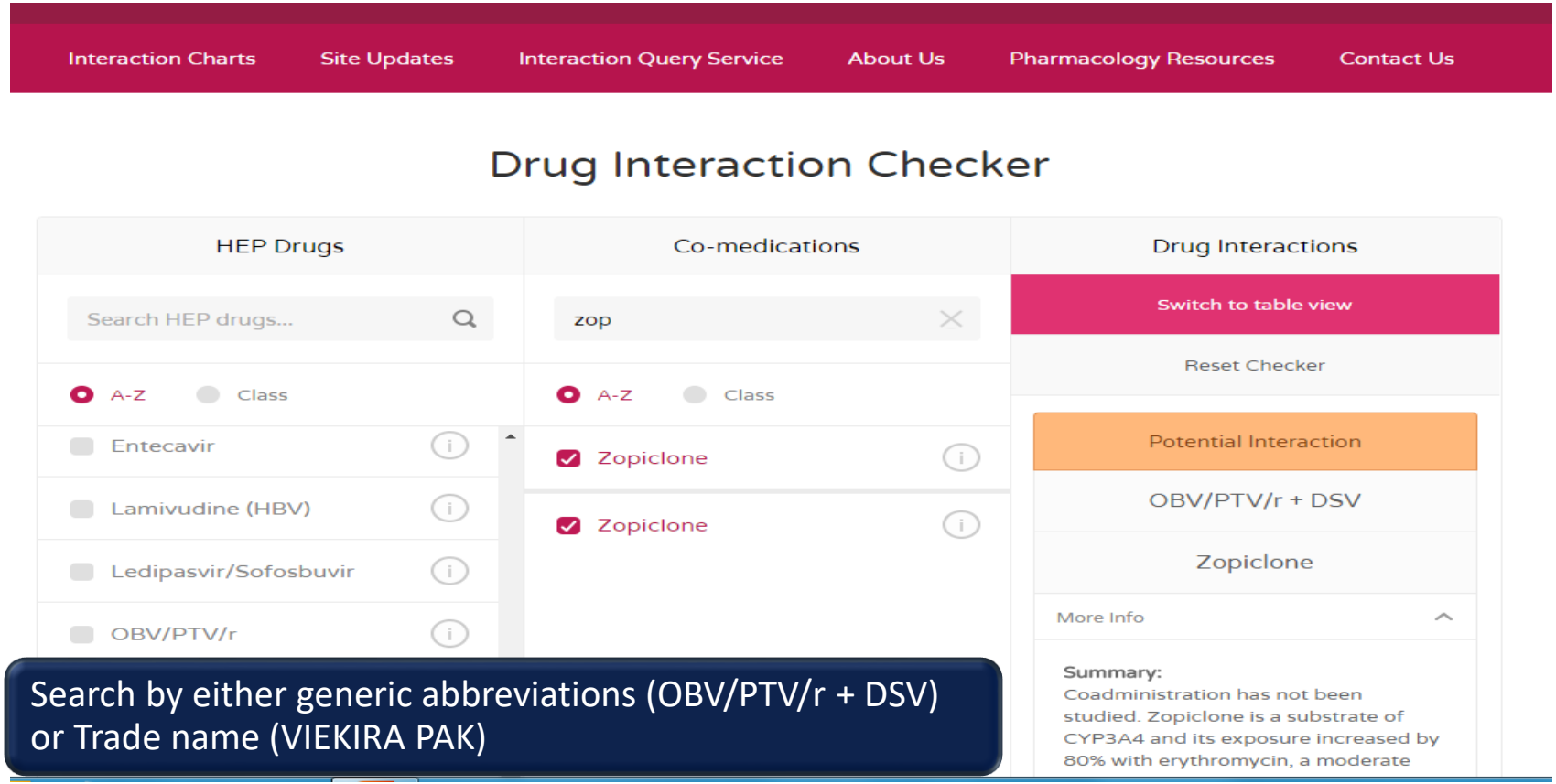


Liverpool HIV & HEPATITIS Pharmacology Group. Hepatitis Drug Interactions. www.hep-druginteractions.org Accessed July 2016.

Example of drug-interaction search: methadone

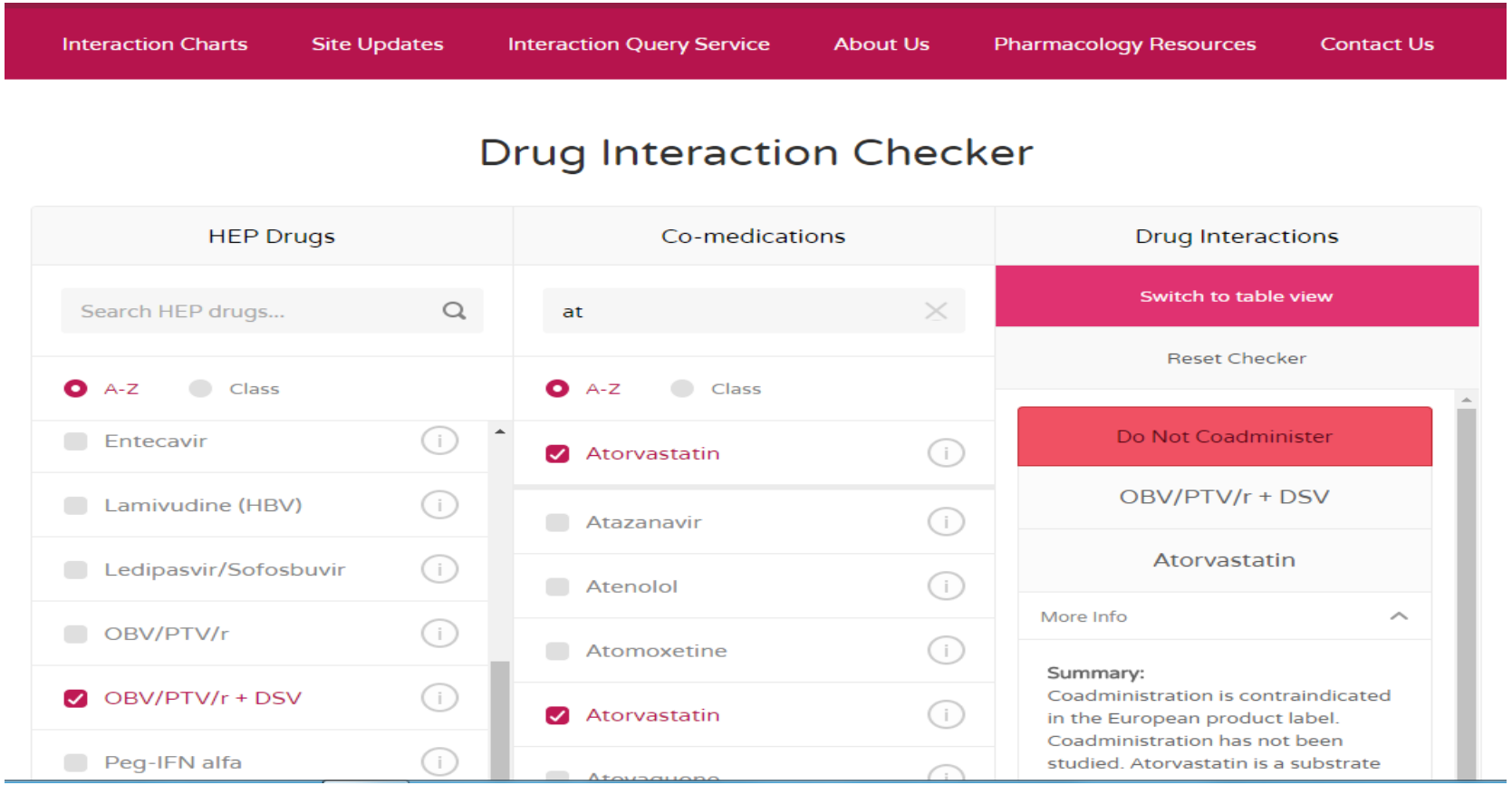


Example of drug-interaction search: zopiclone



Search by either generic abbreviations (OBV/PTV/r + DSV) or Trade name (VIEKIRA PAK)

Example of drug-interaction search: atorvastatin



Summary: VIEKIRA PAK and VIEKIRA PAK-RBV

High certainty of cure*	• EFFICACY: SVR12 = 97% for patients with genotype 1 HCV, including cirrhotics and those who previously failed with pegIFN/RBV.
Low rates of failure	• RESISTANCE PROFILE: Low rates of virologic failure (<2%)
Low rates of discontinuation	SAFETY: Well-tolerated regimen, with low rates of discontinuations due to adverse events (1.0%)

**Cure defined as ≤25 IU/mL HCV RNA 12 weeks after end of treatment (SVR12). SVR12 for VIEKIRA PAK and VIEKIRA PAK-RBV was 97% in patients with GT1 HCV (with or without cirrhosis; pooled analysis Phase III trial cohorts; n=1088).*

AbbVie Limited. VIEKIRA PAK and VIEKIRA PAK-RBV Data Sheets. Medsafe New Zealand; version 10: May 2017.

VIEKIRA PAK and VIEKIRA PAK-RBV are fully funded prescription medicines on the Pharmaceutical Schedule with an alternative Xpharm distribution arrangement. Please review full Data Sheets before prescribing. These are available from AbbVie Limited at www.viekira.co.nz and from Medsafe at www.medsafe.govt.nz.

VIEKIRA PAK is a combination therapy containing ombitasvir/paritaprevir/ritonavir (12.5/75/50/ mg) tablets and dasabuvir (250 mg) tablets. VIEKIRA PAK-RBV contains VIEKIRA PAK, plus ribavirin (200 mg*) tablets.

INDICATIONS: VIEKIRA PAK and VIEKIRA PAK-RBV are indicated for the treatment of genotype 1 chronic hepatitis C (including patients with compensated cirrhosis (Child-Pugh A), co-infection with HIV-1, and those who have had a liver transplant).

CONTRAINDICATIONS: Severe hepatic impairment (Child-Pugh C); Hypersensitivity to components or excipients of VIEKIRA PAK or VIEKIRA PAK-RBV; or Concomitant administration with atorvastatin, carbamazepine, colchicine (in renal or hepatic impairment), efavirenz, ergotamine or its derivatives, ethinyloestradiol-containing medicines (e.g. oral contraceptives), fusidic acid, gemfibrozil, oral midazolam, phenobarbital, phenytoin, ranolazine, rifampicin, St. John's wort (Hypericum perforatum), salmeterol, sildenafil (when used for pulmonary arterial hypertension), simvastatin, terfenadine, or triazolam. Please refer to the full Data Sheets for a complete list of contraindicated medicines. VIEKIRA PAK-RBV: As above, and: Pregnancy, including men whose partners are pregnant (Category X); Severe cardiac disease in previous 6 months; or Haemoglobinopathies (e.g. thalassaemia or sickle-cell anaemia).

PRECAUTIONS: Not recommended for patients with moderate hepatic impairment (Child-Pugh B); For patients with compensated cirrhosis, monitor for clinical signs and symptoms of hepatic decompensation (such as ascites, hepatic encephalopathy, or variceal haemorrhage), and monitor liver function including bilirubin and alanine transaminase (ALT) according to local recommendations; Discontinue treatment in patients who develop evidence of hepatic decompensation or if ALT elevation is accompanied by signs or symptoms of liver inflammation or increasing conjugated bilirubin, alkaline phosphatase, or international normalised ratio (INR); Not recommended for concomitant use with atazanavir/ritonavir, everolimus, fluticasone or other glucocorticoids metabolised by CYP3A, lopinavir/ritonavir, quetiapine, rilpivirine, sirolimus, or tacrolimus; Not recommended for patients with HCV genotypes other than 1; Not studied in patients previously treated with VIEKIRA PAK or other direct-acting antiviral agents; Not studied in patients younger than 18 or older than 70 years; Not recommended in pregnancy (Category B3); Discontinue breastfeeding prior to initiation; and Screen all patients for hepatitis B (HBV) before initiation of treatment and monitor co-infected patients and those with past HBV infection according to current clinical guidelines. VIEKIRA PAK-RBV: As above, and: Obtain a negative pregnancy test prior to initiation of therapy; Ensure patients use two forms of contraception during treatment and for 6 months after treatment (with monthly pregnancy tests during this time); Monitor haemoglobin in patients with pre-existing cardiac disease; Monitor uric acid in patients predisposed to gout; and Reduce dose of ribavirin and monitor haemoglobin in patients with renal impairment.

INTERACTIONS: See Data Sheets for medicines for which dose adjustment and/or monitoring should be considered.

ADVERSE EFFECTS: Fatigue, nausea, pruritus, insomnia and asthenia. **VIEKIRA PAK-RBV:** As above, and: anaemia, diarrhoea, vomiting, decreased appetite, dizziness, headache, sleep disorder, cough, dyspnoea, dry skin, and rash.

DOSAGE AND ADMINISTRATION: The recommended dose is two ombitasvir/paritaprevir/ritonavir (12.5/75/50/ mg) tablets once daily (in the morning) and one dasabuvir (250 mg) tablet taken with food twice daily (morning and evening) for 12 weeks. VIEKIRA PAK-RBV: As above, for 12 or 24 weeks, with ribavirin. The recommended dose of ribavirin depends on a patient's bodyweight (<75 kg = 1000 mg; ≥75 kg = 1200 mg), and should be taken with food in two divided doses (morning and evening). Ribavirin monotherapy is not effective and ribavirin must only be used in combination with VIEKIRA PAK.

See full Data Sheets for additional information on duration of therapy and use in special populations. *Other presentations, including ribavirin 400 mg and 600 mg tablets, are not currently available in New Zealand.