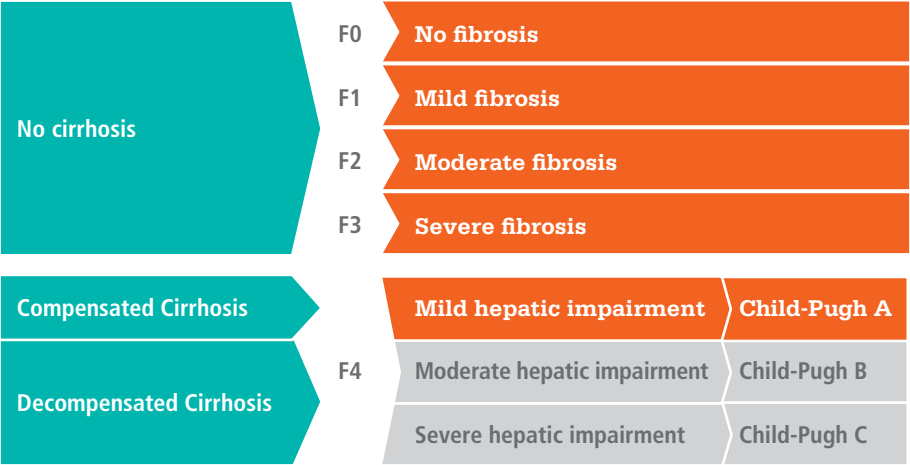


Stages of liver disease⁴



Shading indicates patients for whom VIEKIRA PAK is indicated.^{1,2}



All-oral,
interferon-free^{1,2}

Dose and duration^{1,2}

12 weeks of treatment, either with VIEKIRA PAK or VIEKIRA PAK-RBV, are recommended for most patients.

Patient Population	Treatment	Duration	RBV Daily Dose
GT1b without cirrhosis	VIEKIRA PAK	12 weeks	N/A
GT1a without cirrhosis	VIEKIRA PAK-RBV [†]	12 weeks	<75kg = 1000 mg; ≥75kg = 1200 mg RBV is to be taken in two divided doses, morning and evening.
GT1 with cirrhosis (except GT1a prior null responders) [^]	VIEKIRA PAK-RBV	12 weeks	
GT1a cirrhotic prior null responders [^]	VIEKIRA PAK-RBV	24 weeks	

[†]VIEKIRA PAK without RBV can be considered as a therapeutic option for GT1a HCV without cirrhosis. NOTE: VIEKIRA PAK-RBV is recommended in patients with an unknown GT1 subtype or with mixed GT1 infection.

[^]Prior null responders are people who have previously failed treatment with pegylated-interferon and ribavirin.

Overall cure*
rates in patients
receiving the recommended
dosing regimen in a pooled
analysis of Phase III clinical trials

97%

achieved SVR12^{1,2}

Effectiveness and Tolerability^{1,2}

- 97% of patients achieved cure^{*} in a pooled analysis of Phase III trials^{**}
- All oral, interferon-free
- 12 weeks of treatment for the majority of patients
- Well tolerated with $\leq 1.2\%$ of patients discontinuing therapy due to adverse events

High
certainty
of cure^{*1,2}

^{*} Cure defined as virologic cure, with undetectable HCV RNA (≤ 25 IU/mL) 12 weeks after the end of treatment (Sustained Virologic Response; SVR12)

^{**} The pooled analysis included 1096 patients who received the recommended regimen for their HCV subtype, cirrhosis status, and previous treatment.

Common Side Effects^{1,2}

VIEKIRA PAK: fatigue, nausea, pruritus, insomnia, asthenia, and anaemia.

VIEKIRA PAK-RBV: as above. Patients also reported diarrhoea, vomiting, decreased appetite, dizziness, headache, sleep disorder, cough, dyspnoea, dry skin, and rash.

The more common side-effects are usually mild and short-lived. Patients should seek medical advice without delay if they have symptoms of a severe allergic reaction.

To report an adverse event, please contact AbbVie Pharmacovigilance at drugsafetynz@abbvie.com, and the Centre for Adverse Reactions Monitoring (CARM), carmnz@otago.ac.nz.

Mode of Action^{1,2}

VIEKIRA PAK combines three direct-acting antiviral agents (DAAs) with distinct mechanisms of action to target the hepatitis C virus at multiple steps in its lifecycle. The non-overlapping resistance profiles increase the barrier to resistance.⁵

- **Paritaprevir** is a protease inhibitor, boosted by ritonavir
- **Ombitasvir** inhibits the HCV NS5A protein of the hepatitis C virus
- **Dasabuvir** is an NS5B RNA polymerase inhibitor
- In some types of patients, ribavirin is also added, to maximise response rates (VIEKIRA PAK-RBV).

Drug-drug interactions^{1,2}

The following medicines, which are registered in New Zealand are **contraindicated** with VIEKIRA PAK and VIEKIRA PAK-RBV: **carbamazepine, colchicine** (in renal or hepatic impairment), **efavirenz, ergotamine** and its derivatives, **ethinyloestradiol-containing medicines** (e.g. oral contraceptives), **fusidic acid, gemfibrozil, oral midazolam, phenobarbital, phenytoin, 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.

Coadministration of VIEKIRA PAK and VIEKIRA PAK-RBV may alter the concentrations of a range of concomitant drugs. While some interactions are unlikely to be clinically relevant, others may require clinical monitoring and/or dose adjustments of the concomitant medication.

See Data Sheets for a list of medicines for which dose adjustment or monitoring is recommended. No dose adjustment is needed for VIEKIRA PAK.

Where can I find out more about drug-drug interactions?

The list above is not an exhaustive list of drug-drug interactions; for more information see:

1. Medsafe-approved Data Sheet: www.medsafe.govt.nz
2. University of Liverpool HCV drug interactions website: <http://hep-druginteractions.org/>

Note: VIEKIRA PAK and Ribavirin are listed separately on the website.

3. AbbVie Medical Information: 0800 900 030, medinfoanz@abbvie.com

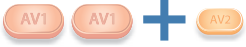



Presentation and packaging

VIEKIRA PAK is provided in a convenient daily blister pack designed for ease of use.

For VIEKIRA PAK-RBV, 200mg ribavirin tablets are provided in plastic bottles of 168 tablets. The bottle of ribavirin tablets is provided inside the VIEKIRA PAK-RBV monthly carton.



Resources for Patients

Each morning	Each evening
VIEKIRA PAK  Take two pink AV1 tablets and one beige AV2 tablet	VIEKIRA PAK  Take one beige AV2 tablet
Ribavirin Take ____ blue tablets 	Ribavirin Take ____ blue tablets 

Tablets are for illustrative purposes only.

AbbVie will provide an information booklet and a dose card for your patient.

Based on your prescription the pharmacist will complete the dose card with the number of ribavirin tablets the patient needs to take each morning and night.

Co-medications.

Ask your patient to tell you about any other medicines they are taking, including recreational drugs and any remedies they buy without a prescription from the pharmacy, supermarket or health-food store.

Important advice for your patient^{1,2}

Pregnancy

VIEKIRA PAK is not recommended; it should only be used in pregnancy if the benefits outweigh the risks (Category B3).

VIEKIRA PAK-RBV: is contra-indicated in pregnancy. Ribavirin must not be used in pregnancy (Category X).

Females and males must use two reliable forms of contraception throughout treatment (progestin-only or non-hormonal methods) with VIEKIRA PAK-RBV and for 6 months after completion of treatment.

Breastfeeding

Patients should discontinue breastfeeding prior to initiation of treatment.

Administration instructions

Tablet should be taken twice daily (morning and evening) at about the same times. Swallow the tablets whole with a glass of water and take with food to maximise absorption.

Missed doses

Inform patients that in case a dose of the pink combination tablet is missed, the prescribed dose can be taken within 12 hours.

If more than 12 hours has passed, the missed dose should NOT be taken.

If a dose of dasabuvir (beige tablet) is missed, the prescribed dose can be taken within 6 hours. If more than 6 hours has passed, the missed dose should NOT be taken.

If a dose of ribavirin is missed, the patient should NOT make up for a missed dose; they should take the next dose as per the usual dosing schedule.

Additional instructions

Your patient should seek medical advice without delay if they have onset of fatigue, weakness, lack of appetite, nausea and vomiting, jaundice or discoloured faeces.

Monitoring during treatment^{1,2}

Monitor changes in laboratory parameters including bilirubin and alanine transaminase (ALT). Discontinue treatment in patients who develop evidence of hepatic decompensation.

In addition, with VIEKIRA PAK-RBV:

- Monitor haemoglobin in patients with pre-existing cardiac disease
- Monitor uric acid in patients predisposed to gout
- Reduce dose of ribavirin and monitor haemoglobin in patients with renal impairment.

Guidelines on reduction of ribavirin dose^{1,2}

If dose adjustment of ribavirin is required because of treatment-emergent anaemia, the number of 200mg ribavirin tablets can be reduced. The patient should be advised, and their dose card should be updated with the change in dose.

Laboratory values	Reduce daily ribavirin dose to 600mg/day* if:	Discontinue ribavirin if: **
Patients with no cardiac disease	Haemoglobin <100 g/L	Haemoglobin <85 g/L
Patients with history of stable cardiac disease	>20 g/L decrease in haemoglobin during any 4-week period during treatment (permanent dose reduction)	Haemoglobin <120 g/L despite 4 weeks at reduced dose

*Patients whose dose of ribavirin is reduced to 600 mg daily should receive one 200 mg tablet in the morning and two 200 mg tablets in the evening.

**If the abnormality is reversed, ribavirin may be restarted at 600 mg daily, and further increased to 800 mg daily at the discretion of the treating physician. However, a return to higher doses is not recommended.

Additional monitoring for patients with cirrhosis^{1,2}

For patients with cirrhosis, monitor for clinical signs and symptoms of hepatic decompensation (such as ascites, hepatic encephalopathy, variceal haemorrhage). Perform hepatic laboratory testing including direct bilirubin levels at baseline, during the first 4 weeks of starting treatment and as clinically indicated thereafter. **Discontinue treatment in patients who develop evidence of hepatic decompensation.**

End of treatment

At the end of treatment, the patient should be instructed to return any unused medication to their pharmacy for disposal.

12 weeks after the end of treatment, perform qualitative PCR to confirm that the patient has achieved a sustained virologic response (SVR12).⁴

REFERENCES: 1. VIEKIRA PAK Data Sheet 30 May 2016 2. VIEKIRA PAK-RBV Data Sheet. 30 May 2016 3. PHARMACEUTICAL SCHEDULE www.pharmac.govt.nz/tools-resources/pharmaceutical-schedule/ 4. Gastroenterological Society of Australia. Australian recommendations for the management of hepatitis C virus infection: a consensus statement 2016. Melbourne: Australia: 2016. 5. Krishnan, Antimicrobial Agents Chemother. 2015 Sep; 59(9): 5445-5454.