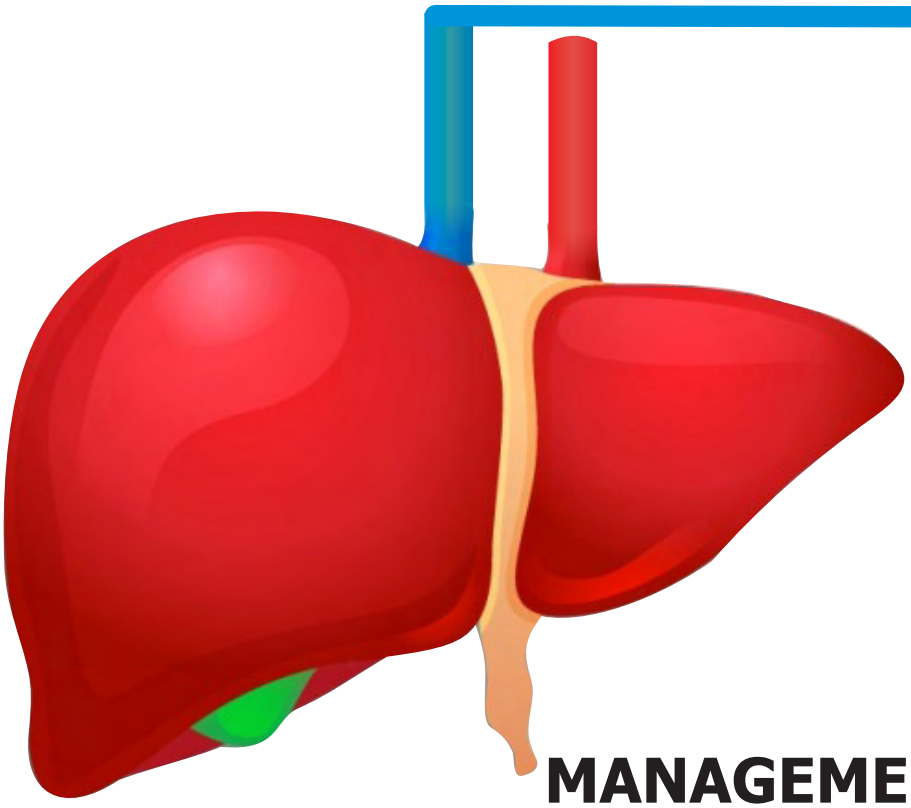
Desk Guide



MANAGEMENT of Chronic Hepatitis C & B

Hepatitis & Infection Control Program
Primary & Secondary Healthcare Department, Punjab

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About this desk guide

Welcome to this practical guide to the diagnosis, treatment and management of chronic Hepatitis C and B cases. It is intended for use by doctors in general medicine and hepatitis clinics in (sub)district hospitals in Pakistan.

It has been produced by the Hepatitis & Infection Control Program, Primary and Secondary Healthcare Department, Punjab, in partnership with the Association for Social Development (ASD); Nuffield Centre, University of Leeds; and key technical partners (PHRC, WHO, PGMI), through COMDIS-HSD (DFID-supported consortium for enhanced service delivery).

1. **Identify at-risk individual for rapid testing**

Note if patient has had:

Ear/nose pierced or tattooing done?

Ask if patient has (or had):

Been injected during the last one year?
From where and how frequent?

Had an outpatient medical, surgical or dental procedure?
What procedure and from where?

Ever been hospitalized?
Where and for what?

Received a blood transfusion?
Where, donor tested (known)?

Frequently get shaving done by a barber?
How long and how frequently?

Ever used injectable drugs?
For how long?

Had unusual urethral discharge; genital sore(s) or ulcer(s); or painful urination or sex?
Ask about history of multiple sex partners.

A family member known to be a case of HCV or HBV?
Who; diagnosed and treated where; and outcome?

Examine and check records:

- Clinically examine for dental extraction, injection marks, STI signs (as relevant)
- Check records (if available) for recorded risk factors (as relevant/available)

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2. **Diagnose HCV / HBV positive cases**

RAPID test results: interpret and respond

Record results in HCV/HBV laboratory register	**If negative:** • counsel about test results; and relevant preventive measures, including HBV vaccination **If positive:** • counsel about test results and further steps • arrange the confirmatory testing (if consent)

CONFIRMATORY test results: interpret and respond

Record results in HCV/ HBV laboratory register	**If negative:** • counsel about test results and preventive measures **If positive:** • counsel about test results and further steps • vaccinate for HBV • decide the priority for program treatment
Prepare treatment card or enter into the deferred treatment register according to treat or not decision (see section 3).	

3. **Assess for HCV/ HBV treatment eligibility**

Examine for <u>decompensated cirrhosis:</u>	**If decompensated HCV:**
a. H/o gastro-intestinal bleed (varices) b. signs of ascites, and **c.** signs of (hepatic) encephalopathy	• refer for specialist assessment/management (i.e. conservative) **If compensated HCV or de/ compensated HBV:** • consider anti-viral treatment

- **Do blood CBC & liver functions: ALT & AST**
- **Calculate the APRI score (as follows):**

(AST / ULN) x 100 / platelet count
Normal ranges: AST: 10 – 40 (IU/L), Platelets: 150– 450 $10^9/L$)
AST: Aspartate aminotransferase; IUL: International units/liter *ULN: Upper limit of normal of AST; Platelet count in billion/ liter*

Interpret APRI score	**Staging of liver fibrosis/cirrhosis**	**Treatment priority**	
		HCV	**HBV**
≥ 2 (Severe disease)	Cirrhosis	Treat as cirrhotic	Prioritize for treatment
1 - < 2 (Moderate disease)			<u>Treat if</u>: • Persisting abnormal ALT (men:>30; women:>20); and • HBV-DNA ≥ 20,000 IU/ml <u>Defer if</u>: • Do not qualify the criteria
< 1 (Mild disease)	Fibrosis (but no cirrhosis)	Treat as non-cirrhotic	

4. **Assess/manage for co-existing conditions**

Check for	Manage
Known allergy to anti-viral drugs (clinical)	• Donot prescribe the culprit drug(s) • Administer first dose under supervision • Refer to specialist, if needed.
Pregnancy test/ breastfeeding in married woman of child bearing age	**If pregnant or breastfeeding:** • Delay anti-HCV until breastfeeding ends • Administer anti-HBV (Tenofovir) **If not pregnant and not breastfeeding**: • Start anti-HCV or anti-HBV; also • If HCV – offer contraception (during and 6 months after the HCV treatment)
Hyperglycemia (RBG>200);and **Hypertension (BP>140/90)**	**If found diabetic or hypertensive:** • Control the disease (use the NCD program guide); then • Start anti-viral (when control achieved) • Refer if disease remains uncontrolled
Low leukocyte count (<2.5x10^9/L) or low platelet count (<90 x10^9/L)	**If leukocytopenia or thrombocytopenia:** • Administer anti-viral (anti-HCV without RBV); also get expert opinion • Monitor fortnightly; refer if severe or non-responding
Moderate or severe proteinuria (2^+- 3^+; ≥4^+) or GFR reduction (30 -59; <30 ml/min)	**If moderate renal impairment:** • If HCV: Sofosbuvir + Daclatasvir (or RBV) • If HBV: Entecavir; or Tenofovir (low dose) • Monitor fortnightly (proteinuria etc.) **If severe impairment: r**efer to a specialist
Depression or psychosis or epilepsy	**If severe mental condition found:** • Control the mental condition; then • Start anti-viral (when control achieved) • Refer if disease remains uncontrolled

Autoimmune dis.; organ transplant; severe disease	**If any of the three conditions (clinical):** • Refer for specialist care
Thyroid disease (clinical and TSH)	**If thyroid disease:** • Start anti-HCV or anti-HBV; also • Treat for thyroid disease
TB (clinical &AFB or Xpert test)	• Treat TB (monitor liver functions); then • Start anti-HCV or anti-HBV
Co-infection: HCV-HBV	• Complete anti-HCV first; then • Treat HBV; or monitor HBV reactivation
Co-infection: HIV with HCV or HBV	• Refer to ART (especially if decompensated liver; or CD4 count ≤ 500 cells/mm^3); also • Refer for expert start of anti-HCV/ HBV
Co-infect: HBV-HDV	• Test HDV immune-globulins (if available)
(Mainly for HCV)	
Low hemoglobin (men: <13g/dL; women: 12 g/dL)	**If Hb is > 10g/dL:** • Start anti-HCV; and monitor fortnightly **If Hb is 8.5 - 10g/dL:** • Reduce RBV (600mg); monitor fortnightly **If Hb is < 8.5g/dL:** • Stop RBV; refer to specialist
COPD (clinical: severity/ control)	• Control COPD (use NCD guide); then • Start anti-HCV regimen (without RBV) • Refer if COPD control is not achieved
Heart failure (Clinical)	**If heart failure found:** • Control the heart failure; then • Start anti-HCV (when control achieved) • Refer if heart fail remains uncontrolled
Significant coronary artery disease(clinical)	**If coronary artery disease found:** • Start anti-HCV; and monitor fortnightly • Refer if coronary disease is uncontrolled

5a. **Prescribe anti-HCV regimen**

HCV: Three regimen available for prescribing are:

- **Twelve or twenty four week regimen**
  - **S**ofosbuvir 400 mg OD (tablet)
  - **D**aclatasvir 60mg OD
- **Twelve week alternate regimen**
  - **S**ofosbuvir + Velpatasvir 400/100mg OD (tablet)
- **Twenty four week regimen (for adolescent)**
  - **S**ofosbuvir 400 mg OD (tablet)
  - **R**ibavirin 800 – 1200 mg OD (as per body weight)
    - ✓ < 60kg: 800 mg per day
    - ✓ 60 - 74 kg: 1000mg per day
    - ✓ ≥ 75 kg: 1200mg per day

The anti-HCV regimen is selected[#] as below:

No cirrhosis (without or with past treatment)	Preferred • 12 week Sofosbuvir & Daclatasvir Alternate • 12 week **S**ofosbuvir + Velpatasvir
Compensated cirrhosis (without or with past treatment)	Preferred • 24 week Sofosbuvir & Daclatasvir Alternate • 12 week Sofosbuvir + Velpatasvir
Decompensated cirrhosis	Add Ribavirin to: • 24 week Sofosbuvir & Daclatasvir or • 12 week Sofosbuvir + Velpatasvir
Adolescent (age: 12–17 year; or weight ≥ 35kg)	• 24 week Sofosbuvir & Ribavirin

 # Anti-HCV regimen is selected on the basis of: a) liver cirrhosis (or not), b) patient age (adolescent or adult); and c) drug availability.

Ideal body weight = 50kg + 2.3 for each inch over 5 ft.

5b. **Prescribe anti-HBV regimen**

Anti-HBV regimen reduces morbidity/mortality but mostly does not achieve cure; thus long-term therapy is required.

Normal or mildly impaired renal function (GFR#: >50)

Drug#	**Dosage (every day)**
Compensated Liver	
Tab. Tenofovir (300 mg)	One tablet per day
Tab. Entecavir (0.5 mg)	One tablet per day
Decompensated Liver	
Tab. Entecavir (0.5 mg)	Two tablets per day

#: select single drug regimen, as per clinical & stock consideration

Moderately impaired renal function (GFR#: 30 – 49)

Drug#	**Dosage**		
	Daily	**or**	**Alternate days**
Compensated Liver			
Tenofovir	4 scoop (powder)		One tablet
Entecavir	0.25mg (oral sol.)		One tablet
Decompensated Liver			
Entecavir (0.5 mg)	One tablet		Two tablets

Severely impaired renal function (GFR#< 30):

- Refer for specialist care.

#: GFR

$$\frac{(140 - \text{age}) \times (\text{ideal body weight in kg}) \text{ for men}}{(72) \times (\text{serum creatinine, mg/dl})} \quad (\text{if woman: X } 0.85)$$

6a. **Follow up of registered HCV cases**

On routine monthly follow-up visits, for each patient:

Clinically assess	• adherence to drug intake (interview and blister count) • anemia; ascites; reported complaints/ side effects
Investigate (if RBV-containing regimen)	• CBC (Hb., WBC and platelet count) • ALT (altered: male ≥30; female≥20) • Also do albumin, bilirubin & coagulation (INR) – if decompensated cirrhosis
Assess and investigate for co-morbid condition	• clinically assess for known: HTN/CVD, DM, renal impairment etc. • Investigate as required for the known co-morbidity e.g. RBG, proteinuria
Prescribe and dispense drugs:	• If pan-genotype anti-HCV regimen: ○ one month pan-genotype drugs ○ one-month co-morbidity drugs, as per program/hospital practice • If RBV-containing regimen: ○ Hb. >10 g/dL: one month normal dose ○ Hb. 8.5 – 10 g/dL: reduce RBV to 600mg/day; monitor Hb. fortnightly • HBV vaccine shot, as schedule
Educate patient	• counsel on adherence; also prevention • update the HCP recommended records
Stop drugs and refer if:	• In RBV-containing regimen, if: ○ Hb. < 8.5 g/dL (please see footnote) ○ signs of liver deterioration or ○ worsening decompensation

Stable CVD: reduce RBV if Hb decreases by ≥ 2 g/dL in 4 weeks; if Hb remains <12 g/dL after 4 weeks of reduced dose - stop RBV.

6b. **Follow up of registered HBV cases**

On routine 3 monthly follow-up visits, for each patient:

Clinically assess (every quarter) for:	• adherence to drug intake (interview/count) • clinical: ascites; coagulopathy, edema, jaundice, complaints/ side effects • known co-morbidity: HTN/CVD, DM etc
Investigate	
Every 3 months for:	• **ALT** (raise in serum levels) • If co-morbidity – as required e.g. RBG (DM)
Every 6 months for:	• **CBC**(leukocyte and platelet count) • If known moderate renal disease or DM/HTN: do proteinuria • If risk of liver decompensation: serum albumin, bilirubin & coagulation (INR)
Every 12 months for:	• At every 12 month completion: HBV-DNA ○ if HBV-DNA not detected: stop therapy ○ if inadequate response: stop therapy & refer • **APRI score**(for cirrhosis progression) • If known mild(no) renal disease and no DM/HTN): do proteinuria • If known≥ 2^{+}or DM/HTN: GFR(if available) • If family history of hepato-cellular cancer or age ≥40 years: do ultrasound and AFP
Manage:	
Prescribe and dispense drugs:	• Three months of anti-HBV drug; dosage as per liver and renal functions • drug for co-morbidity, as per hospital practice
Educate patient	• counsel on adherence; also prevention • update the HCP recommended records
Refer if:	• de-compensation or disease progression

Note: The above follow-up schedule does not cover all special follow-up needs related to the co-morbid conditions.

7. **Treatment adherence and outcomes**

7.1 Adherence (both C & B): At the end of each month**:**

Identify non-adherence to follow-up visits:	• manually: three-tray system; or • electronic: HCP software (if available)
Take retrieval action:	• reminder SMS or phone-call or • visit by healthcare staff
Manage the cases retrieved (after interruption)	If interruption is: • < 15 days: continue the treatment • > 15 days: reassess; then restart (HCV) or continue(HBV) treatment

7.2a Treatment Outcome Hepatitis C

- Get PCR done after 12 weeks of completed treatment

Considerations		**Treatment outcome**
Drugs taken	**Others**	
12 or 24 weeks#	-	Completed
	SVR-12 achieved	Successful treated
<12 or 24 weeks#	Liver decompensation	Stopped (for clinical reason)
	Interrupt > 15 days	Lost to follow-up
	Report: family/contact	Died
SVR: PCR repeated 12 weeks after successful treatment completion.		

drug intake duration varies as per cirrhosis (or not) and prescribed regimen.

7.2bTreatment Response Hepatitis B

Two-year cohorts of patients receiving treatment are quarterly assessed (i.e. continued, stopped, defaulted, died); and reported.

Developed by:

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