Prescribing Protocol – SESLHDPR/726
Entecavir for HBV reactivation in Renal Patients

Health
South Eastern Sydney
Local Health District

Title	Entecavir as prevention of Hepatitis B virus (HBV) reactivation in at risk **renal patients** receiving immunosuppressive therapy.
Areas where Protocol/Guideline applicable e.g. District, Hospital, ITU, Ward	SESLHD
Authorised Prescribers	Renal, Gastroenterology, Infectious Diseases
Indication for use	Prevention of HBV reactivation in moderate to high risk **renal patients** receiving immunosuppressive therapy. *For haematology/oncology patients receiving cancer therapy refer to eviQ Clinical resource: Hepatitis B virus prophylaxis in immunocompromised adults.*
Clinical condition	Investigations: HBV surface antigen (HBsAg), HBV surface antibody (HBsAb), HBV core antibody (anti-HBc), HBV DNA Inclusion criteria: 1. HBsAg and/or DNA positive. *This is consistent with active disease (acute or chronic hepatitis B). Gastroenterology/ID must be consulted.* 2. HBsAg negative and anti-HBc positive **AND** receiving B cell-depleting, B-cell active or anti-CD20 therapy (e.g. Rituximab) **For kidney transplant recipients (HBsAg and DNA negative):** • anti-HBc positive kidney donor (past infection) with non-immune recipient (HBsAb <100IU/L) • anti-HBc positive kidney recipient (past infection) with HBsAb <10IU/L Note: HBsAg negative and anti-HBc positive patients NOT receiving high-risk immunosuppression outlined in (2) may be moderate risk and require consultation with Gastroenterology or Infectious Diseases.
Contra-indications	Previously demonstrated hypersensitivity to entecavir or tablet excipients (note: tablets contain lactose) Lamivudine-exposure – do not use entecavir because cross-resistance is common
Precautions	Coinfection with HIV - avoid entecavir unless treated concurrently with antiretroviral
Place in Therapy	First line.

<table>
<tr><td>Dosage</td><td>0.5 mg ONCE daily
Dosage adjustment required for renal impairment
<table>
<tr><th>Creatinine clearance (mL/min)</th><th>Entecavir dose</th></tr>
<tr><td>30 - 49</td><td>0.25 mg ONCE daily or
0.5 mg every 48 hours</td></tr>
<tr><td>10 - 29</td><td>0.5 mg every 72 hours</td></tr>
<tr><td>< 10</td><td>0.5 mg every 5 – 7 days</td></tr>
<tr><td>Haemodialysis or CAPD</td><td>0.05 mg ONCE daily or
0.5 mg every 5 – 7 days</td></tr>
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No dosage adjustment required for hepatic impairment</td></tr>
<tr><td>Duration of therapy</td><td>Ideally commence 1 week prior to intense immunosuppressive therapy (but should not delay transplant or commencement of immuno- or chemo-therapy)

Duration of therapy based on clinical condition.
<table>
<tr><td>18 – 24 months</td><td>After completion of intense immunosuppressive therapy (e.g. B cell-depleting, B cell active, anti-CD20 therapy, or kidney transplant recipients that receive thymoglobulin and/or rituximab for treatment of acute cellular and/or antibody mediated rejection in their post-transplant course)</td></tr>
<tr><td>12 months</td><td>Post renal transplant who are HBcAb positive, or received a transplant from HBcAb positive donor, who meet criteria outlined above in clinical condition</td></tr>
<tr><td>Indefinite</td><td>Post-transplant recipients who are HBsAg positive and/or DNA positive (i.e. have acute/chronic hepatitis B), these patients must be referred and managed by gastroenterology/ID</td></tr>
</table>
Recommendations on the duration of antiviral prophylaxis differ across international guidelines. The above should be used as a general guidelines, but the timing of cessation of antiviral therapy should be individualised and left to the discretion of the hepatologist. The duration of treatment is to be dependent on clinical judgement and on a case-by-case basis.</td></tr>
<tr><td>Important Drug Interactions</td><td>Nil significant.</td></tr>
<tr><td>Administration instructions</td><td>Swallow tablet whole on an empty stomach (at least 2 hours after a meal and at least 2 hours before the next meal).</td></tr>
<tr><td>Monitoring requirements</td><td>ALT, HBsAg and HBV DNA level every 3 months and HBV serology annually for duration of therapy through to 12 months after cessation of HBV prophylaxis.
Renal function for potential dose adjustment.</td></tr>
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Basis of Protocol/Guideline (including sources of evidence, references)	1. British Transplantation Society Guidelines for Hepatitis B and Solid Organ Transplantation. January 2018 2. Solid Organ Transplantation from Hepatitis B virus positive donors: consensus guidelines for recipient Management. (2015) 3. National Comprehensive Cancer Network (NCCN) 2018 Prevention and Treatment of Cancer-Related Infections 4. New England Journal of Medicine (2006) A Comparison of Entecavir and Lamivudine for HBeAG-Positive Chronic Hepatitis B 5. American Medical Association (2014) Entecavir vs. Lamivudine for Prevention of Hepatitis B Virus Reactivation Among Patients With Untreated Diffuse Large 8-Cell Lymphoma Receiving R-CHOP Chemotherapy 6. Liver International (2013) Entecavir versus lamivudine for hepatitis B prophylaxis in patients with haematological disease 7. Loomba, R., and Liang, T.J., Gastroenterology (2017) Hepatitis B Reactivation Associated with Immune Suppressive and Biological Modifier Therapies: Current Concepts, Management Strategies, and Future Directions 8. Hicks, L.K., Lien, K., and Chan, K.K.W., American Society of Clinical Oncology (2015) ASCO Provisional Clinical Opinion for Hepatitis B Virus Screening Before Cancer Therapy: Are These the Right Tests in the Right Patients? 9. Perrillo, R.P., Gish, R., and Falck-Ytter Y.T., American Gastroenterological Association (2015) American Gastroenterolooical Association Institute Technical Review on Prevention and Treatment of Hepatitis B Virus Reactivation During Immunosuppressive Drug Therapy 10. Reddy, K.R., Beavers, K.L., Hammond, S.P., Lim, J.K., and Falck-Ytter, Y.T., American Gastroenterological Association (2015) American Gastroenterological Association Institute Guideline on the Prevention and Treatment of Hepatitis B Virus Reactivation During Immunosuppressive Drug Therapy 11. Terrault, NA, Lok, A S.F., McMahon, B.J., Change, K., Hwang, J.P., Jonas, M.M., Brown Jr, R.S., Bzowel, N.H., and Wong, J. B (2018) American Association for the Study of Liver Disease. Update on Prevention, Diagnosis, and Treatment of Chronic Hepatitis B: MSLD 2018 Hepatitis B Guidance 12. Taplitz, R.A., Kennedy, E.B., Bow, E.J., Crews, J., Gleason, C., Hawley, D.K., Langston, A.A, Nastoupil, L.J., Rajotte, M., Rolston, K.V., Strasfeld, L., and Flowers, C.R. (2018) Journal of Clinical Oncology. Antimicrobial Prophylaxis for Adult Patients With Cancer Related Immunosuppression: ASCO and IDSA Clincal Practice Guideline Update 13. Australian Medicines Handbook (2019) entecavir 14. MIMsOnline (2018) entecavir (Baraclude) 15. eTG (2021) Hepatitis B 16. Hepatitis B Management during Cancer Therapy Consensus Statement Group 2019. Hepatitis B management during immunosuppression for haematological and solid-organ malignancies: an Australian consensus statement 2019. Melbourne: Hepatitis B Management during Cancer Therapy Consensus Statement Group.
Groups consulted in development of this protocol	Infectious Diseases Department

AUTHORISATION	
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GOVERNANCE	
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