

DATE:	2022 May 30
TO:	All Health Care Providers
FROM:	Alberta Precision Laboratories (APL) – Public Health Laboratory
RE:	Albendazole level monitoring in treatment of AE (alveolar echinococcosis)

PLEASE POST OR DISTRIBUTE AS WIDELY AS APPROPRIATE

Key Message

- Alveolar echinococcosis (AE) is a life-threatening zoonosis caused by *Echinococcus multilocularis* with mortality rates approaching 90% at 10-15 years, if untreated/inadequately treated
- Treatment includes surgery and /or long-term treatment with albendazole (ABZ), a broad-spectrum benzimidazole
- WHO recommends ABZ treatment for a minimum of 2 years, if complete surgical resection of lesions is performed, and lifelong in virtually all other circumstances
- ABZ levels must be monitored in patients on long term treatment to ensure efficacy and prevent hepatotoxicity and bone marrow suppression.

Background

- AE presents as continuously growing tumour-like liver mass, with local or metastatic spread to distant organs. To date 21 cases were diagnosed in Alberta (the majority of the cases in North America).
- Treatment of AE relies on chemotherapy with or without surgery depending on factors such as size and location of the parasite, its viability, host status etc
- If surgery is carried out, it is always accompanied by chemotherapy with benzimidazoles, usually albendazole (and if not tolerated, mebendazole), continued for **at least 2** years thereafter. Inoperable cases undergo long-term, often life-long, treatment. Clinical studies have shown that benzimidazoles have significantly increased the survival rate despite its variable and a relatively narrow therapeutic index
- Long term use of benzimidazoles can be associated with serious hepatotoxicity and bone marrow toxicity. Albendazole and mebendazole exhibit a parasitostatic rather than a parasitocidal effect and recurrence/relapse rates of AE are relatively high if therapeutic drug concentrations are not maintained because of variable drug absorption or toxicity-driven interruption of treatment. Therefore, maintenance of appropriate therapeutic window is essential, and albendazole levels should be monitored in AE patients, particularly those with progressive diseases or underlying conditions such as immunosuppression.

Ordering and collection guidelines:

Testing is available province-wide for confirmed cases of AE, when ordered by an ID physician

Restricted – Microbiologist on call approval required UNLESS PREVIOUSLY ARRANGED BY CONSULTATION

- **Initiation of therapy:**
 - Testing frequency
 - 1, 4 and 12 weeks after start of treatment
 - 2-4 weeks post each dose adjustment



- **Monitoring of ongoing therapy:**
 - Testing frequency
 - At least once a year, or more often (suspected non adherence, dietary changes, other drug interactions or with any increase in transaminases or size of the lesion)
 - 2-4 weeks post each dose adjustment
 - *Note: each dose should be taken with a fatty meal.*
- **Blood collection:** 4 hours post dose
 - Specimen type: serum (**red top, any tube without gel**)
 - Optimal specimen volume: 2-2.5 mL of serum (minimum 1 mL)

Transport with cold packs or dry ice to APL-Public Health Laboratory (ProvLab Edmonton) “Attn. Parasitology/MOC”

For details, see

<https://www.albertahealthservices.ca/webapps/labservices/indexAPL.asp?id=9324&tests=&zoneid=1&details=true>

Interpretation of levels:

Albendazole is converted to albendazole sulfoxide by first-pass metabolism and the result is reported as concentration of pharmacologically active metabolite albendazole sulfoxide with ranges as follows:

- Therapeutic range: 1.6 – 6.0 µmol/L
- Reduce the dose if two consecutive levels are above 10 µmol/L

The parent component albendazole should not be measurable in the serum. However, if albendazole concentration is detectable at ≥30% of that of albendazole sulfoxide in the sample, it may indicate inappropriate time of collection, or impaired drug metabolism such as decreased liver function, drug interactions etc.

Actions required

- Refer to the above guidelines when treating patients with AE and share this information with relevant stakeholders when necessary
- Work closely with Infectious Diseases (province-wide) and ensure clear and prompt communications with the APL-Public Health Laboratory on-call team throughout the process
- For urgent queries regarding sample collection page APL Provincial Lab Microbiologist on Call (780-407-8822)

Inquiries and feedback may be directed to

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Approved By

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