DIFUMATE™ -120 / DIFUMATE™-240

(Dimethyl Fumarate Delayed-Release Capsules USP, 120 mg and 240 mg)

COMPOSITION: Each hard gelatin capsule of DIFUMATE™ -120 and DIFUMATE™-240 contains dimethyl fumarate USP, 120 mg or dimethyl fumarate USP, 240 mg respectively. **DESCRIPTION:** DIFUMATE™ -120 have an opaque green cap printed "AN" on cap with black ink and opaque **white body** printed "1318" on body with black ink and DIFUMATE™-240 have an opaque green cap printed "AN" on cap with black ink and opaque **green body** printed "1319" on body with black ink. **PHARMACOTHERAPEUTIC GROUP**: Immunosuppressants, other immunosuppressants. **ATC CODE:** L04AX07. **INDICATIONS:** Indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults. **DOSAGE AND ADMINISTRATION:** The starting dose for dimethyl fumarate delayed-release capsules are 120 mg twice a day orally. After 7 days, the dose should be increased to the maintenance dose of 240 mg twice a day orally. Temporary dose reductions to 120 mg twice a day may be considered for individuals who do not tolerate the maintenance dose. Within 4 weeks, the recommended dose of 240 mg twice a day should be resumed. Discontinuation of dimethyl fumarate delayed-release capsules should be considered for patients unable to tolerate return to the maintenance dose. The incidence of flushing may be reduced by administration of dimethyl fumarate delayed-release capsules with food. **Blood Tests Prior to Initiation of Therapy:** Obtain a complete blood cell count (CBC) including lymphocyte count before initiation of therapy. Obtain serum aminotransferase, alkaline phosphatase, and total bilirubin levels prior to treatment with dimethyl fumarate delayed-release capsules. **WARNINGS & PRECAUTIONS:** Dimethyl fumarate can cause anaphylaxis and angioedema after the first dose or at any time during treatment. Signs and symptoms have included difficulty breathing, urticaria, and swelling of the throat and tongue. Progressive multifocal leukoencephalopathy (PML) has occurred in patients with MS treated with dimethyl fumarate. PML has also occurred in the post-marketing setting in the presence of lymphopenia ($< 0.9x10^9$/L). While the role of lymphopenia in these cases is uncertain, the PML cases have occurred predominantly in patients with lymphocyte counts $< 0.8x\ 10^9$/L persisting for more than 6 months. Serious cases of herpes zoster have occurred with dimethyl fumarate, including disseminated herpes zoster, herpes zoster ophthalmicus, herpes zoster meningoencephalitis and herpes zoster meningomyelitis. Other serious opportunistic infections have occurred with dimethyl fumarate, including cases of serious viral (herpes simplex virus, West Nile virus, cytomegalovirus), fungal (Candida and Aspergillus), and bacterial (Nocardia, Listeria monocytogenes, Mycobacterium tuberculosis) infections. Dimethyl fumarate may decrease lymphocyte counts. Clinically significant cases of liver injury have been reported in patients treated with dimethyl fumarate in the post-marketing setting. Signs and symptoms of liver injury, including elevation of serum aminotransferases to greater than 5-fold the upper limit of normal and elevation of total bilirubin to greater than 2-fold the upper limit of normal have been observed. Dimethyl fumarate may cause flushing (e.g., warmth, redness, itching, and/or burning sensation). Serious gastrointestinal reactions, including perforation, ulceration, hemorrhage, and obstruction, some with fatal outcomes, have been reported in the post-marketing setting with the use of fumaric acid esters, including dimethyl fumarate, with or without concomitant aspirin use. **PREGNANCY:** Dimethyl fumarate use in pregnant women have not indicated an increased risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. **LACTATION:** The effects on the breastfed infant and on milk production are unknown. The following adverse reactions have been identified during post-approval use of dimethyl fumarate: (1) Gastrointestinal Disorders: Acute pancreatitis; gastrointestinal perforation, ulceration, obstruction, and hemorrhage. *(2)* Hepatobiliary Disorders: Liver function abnormalities. (3) Infections and Infestations: Herpes zoster infection and other serious opportunistic infections. (4) Respiratory, Thoracic, and Mediastinal Disorders: Rhinorrhea. (5) Skin and Subcutaneous: Alopecia. **STORAGE:** Store below 30°C. Protect from light. Store in original container. Capsules should be swallowed whole and not to be chewed or crushed. Keep out of the sight and reach of children. **PRESENTATION:** DIFUMATE™ -120 are available as **7-day bottle of 14 capsules** in HDPE Bottle and DIFUMATE™-240 are available as **14-day bottle of 60 capsules** in HDPE Bottle. **PATIENT COUNSELLING INFORMATION:** Inform patients that they will be provided with two strengths of dimethyl fumarate delayed-release capsules when starting treatment: 120 mg capsules for the 7-day starter dose and 240 mg capsules for the maintenance dose, both to be taken twice daily. Inform patients to swallow dimethyl fumarate delayed-release capsules whole and intact.