dapsone 100 mg orally daily; dapsone 50 mg daily plus pyrimethamine 50 mg orally weekly plus leucovorin 25 mg orally weekly; and dapsone 200 mg orally weekly plus pyrimethamine 75 mg orally weekly plus leucovorin 25 mg orally weekly. Secondary prophylaxis can be ceased after the commencement of antiretroviral therapy and the reconstitution of the CD4 lymphocyte count to > 200 cells/μl for more than 3 months. If PCP occurred when the CD4 lymphocyte count was higher than 200, the current recommendation is to continue prophylaxis for life (National Institutes of Health [NIH], 2015).

#### *TOXOPLASMA GONDII*

Dapsone alone is not recommended as first-line treatment or prophylaxis for *T. gondii* infection in HIV infection. When used in combination with pyrimethamine and leucovorin as one of the regimens outlined earlier for PCP prophylaxis, it is recognized as being effective, but is inferior to TMP–SMX or pyrimethamine–sulfadoxine (Fansidar) (NIH, 2015).

#### ANTI-INFLAMMATORY THERAPY

When dapsone is used for treatment of inflammatory disorders such as dermatitis herpetiformis or epidermolysis bullosa, the usual starting dose in adults is 50 mg/day titrated upward to as much as 300 mg daily until side effects become intolerable. Once the disease has become controlled, the dose should be reduced to the minimum necessary to control skin lesion development. In the case of dermatitis herpetiformis, dapsone acts only on the dermatologic manifestations of the disease and must be combined with a gluten-free diet to control the small intestinal component of the disease (Wolf *et al.,* 2000). Cimetidine at 400 mg three times a day in adults has been used to ameliorate the side effects of dapsone when higher doses are necessary (Coleman *et al.,* 1992).

Topical dapsone gel 5% is recommended to be applied twice daily to the affected skin when treating acne vulgaris in patients 12 years of age and older. Owing to systemic absorption, G6PD status must be determined before use (Draelos *et al.,* 2007).

## 4b. Newborn infants and children

#### *MYCOBACTERIUM LEPRAE*

The dose of dapsone in pediatrics is 1–2 mg/kg/day up to a maximum of 100 mg/day. A liquid formulation is available in some countries; however, a suspension is most frequently formulated by crushing tablets and suspending the powder in a liquid.

#### *PLASMODIUM* INFECTION

Dapsone combinations are now not recommended for therapy or prophylaxis for malaria in children.

#### *PNEUMOCYSTIS JIROVECI* AND *TOXOPLASMA GONDII* INFECTION

In HIV-infected children, a daily dose of 2 mg of dapsone per kilogram per day was more effective as prophylaxis against PCP than 1 mg/kg/day. A weekly dose of 4 mg/kg was less effective than a daily dose of 2 mg/kg but had fewer side effects (McIntosh *et al.,* 1999).

The dose for *T. gondii* prophylaxis in children is 2 mg/kg/day or 15 mg/m$^2$ per day up to 25 mg/day but, as with adults, dapsone alone is not recommended as first-line treatment or prophylaxis for *T gondii* infection in HIV infection.

## 4c. Pregnant and lactating mothers

Dapsone has been widely used in the treatment of leprosy and malaria in pregnant women (all trimesters) and does not appear to pose a risk to the fetus or to the newborn (NPS MedicineWise, 2016). Dapsone has been assigned to US Food and Drug Administration FDA pregnancy category C. No dosage adjustment is required during pregnancy. However, dapsone can cross the placenta and is excreted in breast milk together with its acetyl metabolite such that cases of mild neonatal hemolytic anemia have been reported (Sanders *et al.,* 1982; Edstein *et al.,* 1986; Zuidema *et al.,* 1986) (see section 6, Adverse Reactions and Toxicity).

## 4d. Those requiring altered dosages

#### PATIENTS WITH IMPAIRED RENAL FUNCTION

Caution is recommended when using dapsone in patients with significant renal impairment, although specific studies have not been reported (Brier and Aronoff, 2007). It is recommended that for patients on hemodialysis the dose be reduced to no more than 50 mg twice daily, with a dose given after dialysis (Gupta *et al.,* 2005).

#### PATIENTS WITH IMPAIRED HEPATIC FUNCTION

There are few data regarding the use of dapsone in the setting of hepatic failure. However, it is metabolized by the liver, and serum levels may therefore be expected to increase in patients with reduced hepatic clearance.

#### OBESE PATIENTS

Obesity significantly lowers plasma dapsone trough levels; however, body mass index (BMI) has only a weak association (Moura *et al.,* 2014).

# 5. PHARMACOKINETICS AND PHARMACODYNAMICS

## 5a. Bioavailability

Dapsone is well absorbed after oral ingestion, with a bioavailability of more than 86% (Pieters and Zuidema, 1987). Peak serum concentrations between 1.1 and 2.33 μg/ml are reached after 0.5–4 hours in healthy volunteers, with an elimination half-life ranging from 12 to 30 hours (Pieters and Zuidema, 1986). Twenty-four hours after oral ingestion of 100 mg of dapsone, plasma concentrations range from 0.4 to 1.2 μg/ml. Approximately 70% of the drug is protein bound, and a dose of 100 mg/day produces a steady-state