patient considerations weighing benefit and risks.[151,377] If pyrazinamide is not included in the initial treatment regimen, the minimum duration of TB therapy with isoniazid, rifampin, and ethambutol should be 9 months for drug-susceptible TB **(AII).** The decision regarding whether to include pyrazinamide in treatment regimens during a pregnancy should be made after consultation among obstetricians, TB specialists, and the patient, while considering gestational age and likely susceptibility pattern of the TB strain.

Experience using the majority of the second-line drugs for TB during pregnancy is limited.[378-381] MDR TB in pregnancy should be managed in consultation with a specialist. In a small prospective study of pregnant women who received second-line MDR/RR-TB regimens that contained bedaquiline or delamanid (including linezolid, clofazimine, amikacin, capreomycin, and kanamycin) 98% had successful treatment outcomes, and at least 81% of continued pregnancies resulted in live births with 68% normal birthweight neonates.[378] The following concerns should be considered when selecting second-line anti-TB drugs for use during pregnancy:

- **Bedaquiline:** Data on the use of bedaquiline in pregnancy are limited, but a study of 108 pregnant women from South Africa found an increased frequency of low birthweight (<2,500 g) among children exposed to bedaquiline *in utero* compared to those who were not exposed (45% vs. 26%; $P = 0.034$).[382] The median birthweight between the two groups, however, was not statistically significant (2690 vs. 2900 grams [$P = 0.18$]) and after 1 year, most children exposed to bedaquiline had gained weight and were doing well. Bedaquiline concentrations in breast milk may be as high or higher than concentrations in maternal plasma, which may have implications for the infant.[383,384]
- **Cycloserine:** No data are available from animal studies or reports of cycloserine use in humans during pregnancy.
- **Ethionamide** has been associated with an increased risk for several anomalies in rats after high-dose exposure, but not in mice or rabbits.[385-387] Case reports have documented cases of CNS defects in humans and hypothyroidism, but overall experience is limited with use during human pregnancy.[388] Ethionamide is likely present in the breast milk, which could be associated with thyroid issues in the infant. Thus, ethionamide should be avoided, unless its use is required on the basis of susceptibility testing **(CIII).**
- **Fluoroquinolones:** Because arthropathy has been noted in immature animals exposed to fluoroquinolones *in utero*, quinolones are typically not recommended during pregnancy or for children aged <18 years **(CIII).** However, studies evaluating fluoroquinolone use in pregnant women did not find an increased risk of birth defects or congenital musculoskeletal abnormalities.[389-393] Furthermore, fluoroquinolones were used in a larger South African case series of MDR TB treatment in pregnancy with generally good outcomes.[382] Thus, fluoroquinolones can be used in pregnancy for drug-resistant TB if they are required on the basis of susceptibility testing **(BII).**[394]
- **Linezolid:** Animal studies of linezolid in pregnancy report decreased fetal body weight and increased fusion of costal cartilage.[395] There are few studies in human pregnancy, but linezolid has been used for the treatment of DR-TB in some high-burden countries.[378,382] In these case studies, monitoring complete blood counts for anemia and thrombocytopenia and advising iron supplementation has been recommended.[384,396]
- **Delamanid:** Delamanid appears to be safe in animal reproductive toxicity studies. It has been used in small cohorts of pregnant women for DR-TB with favorable outcomes.[378,397]