

TABLE 2. OVERVIEW<sup>21,30,32,33,37,46,47,48</sup>

Generic name	Brand name	Class	Dose	How supplied	Hepatic or renal dosing
Bosentan	Tracleer®	Endothelin receptor antagonist	62.5 mg twice daily with or without food for 4 weeks, then increase to 125 mg twice daily. Patients < 40 kg: maintain at 62.5 mg twice daily	Oral tablets, 62.5 and 125 mg	Reduce dose and closely monitor in patients whose aminotransferases >3x ULN Avoid in moderate and severe hepatic impairment
Ambrisentan	Letairis®	Endothelin receptor antagonist	5 mg once daily with or without food. Increase to 10 mg once daily if tolerated.	Oral tablets, 5 and 10 mg	Not recommended in moderate to severe hepatic impairment. No adjustments for mild to moderate renal impairment.
Epoprostenol	Flolan®	Prostacyclin analog	Initial: 2 ng/kg/min IV, titrate upward in increments of 2 ng/kg/min every 15 min or longer until dose-limiting effects or tolerance develops; decrease infusion rate if necessary Maintenance: as tolerated	Intravenous powder for solution: 0.5 and 1.5 mg	No suggested dose adjustments for hepatic or renal insufficiency.
Treprostinil (subcutaneous injection)	Remodulin®	Prostacyclin analog	Initial: 1.25 ng/kg/min (or 0.625 ng/kg/min if not tolerated); titrate based on clinical response by increasing dose in increments of 1.25 ng/kg/min per week for the first 4 weeks of treatment, later 2.5 ng/kg/min per week Transition from epoprostenol: start at 10% of current epoprostenol dose	Subcutaneous injection solution (20 mL vials): 1 mg/mL, 2.5 mg/mL, 5 mg/mL, and 10 mg/mL	Initial dose of 0.625 ng/kg/min ideal body weight for mild to moderate hepatic insufficiency No studies performed in severe hepatic insufficiency
Treprostinil (inhalation)	Tyvaso®	Prostacyclin analog	Initial: 3 breaths (18 mcg) per treatment session; may reduce to 1 or 2 breaths if not tolerated. Maintenance: titrate to 9 breaths (54 mcg) per treatment session as tolerated Four treatment sessions each day, approximately four hours apart during waking hours	Sterile solution for oral inhalation: 2.9 mL ampule containing 1.74 mg treprostinil (0.6 mg per mL)	No specific dose adjustments recommended.
Iloprost	Ventavis®	Prostacyclin analog	Initial: 2.5 mcg per dose, increase to 5 mcg if tolerated. Six to nine inhalation sessions per day, no more than once every 2 hours	Single-use glass ampules for inhalation (1 mL): 10 mcg/mL and 20 mcg/mL	No studies performed in hepatic or renal insufficiency

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Tadalafil	Adcirca®	PDE5 inhibitor	40 mg once daily, with or without food	Oral tablet, 20 mg	Avoid use in severe hepatic or renal impairment. No dose adjustments for mild or moderate impairment.
Sildenafil	Revatio®	PDE5 inhibitor	20 mg orally 3 times daily; give doses approximately 4 to 6 hr apart. With or without food	Oral tablet, 20 mg	No adjustments
PDE5: phosphodiesterase-5 ULN: upper limit of normal					

**TABLE 3. ADVERSE EVENTS, PRECAUTIONS, CONTRAINDICATIONS, AND DRUG INTERACTIONS**

	Adverse events	Precautions	Contraindications	Drug Interactions
<b>Bosentan</b>	Common: respiratory tract infection, anemia Serious: Potential liver injury, fluid retention	<ul style="list-style-type: none"> <li>• Pre-existing hepatic impairment</li> <li>• Fluid retention may require intervention</li> <li>• Decreased sperm counts</li> <li>• Decreased hemoglobin and hematocrit may require monitoring</li> <li>• Pulmonary veno-occlusive disease</li> </ul>	<ul style="list-style-type: none"> <li>• Boxed warning: Birth defects if used during pregnancy</li> <li>• Concurrent use with Cyclosporine A</li> <li>• Concurrent use with glyburide</li> <li>• Hypersensitivity to bosentan</li> </ul>	<ul style="list-style-type: none"> <li>• Hormonal contraceptives: reduced contraceptive effectiveness</li> <li>• CYP3A-metabolized statins: decreased statin levels</li> <li>• Rifampin: alters bosentan levels; monitor hepatic function</li> </ul>
<b>Ambrisentan</b>	Common: peripheral edema, nasal congestion, sinusitis, flushing, palpitations, nasopharyngitis, abdominal pain, and constipation Serious: Potential liver injury, fluid retention	<ul style="list-style-type: none"> <li>• Decreased hemoglobin within the first few weeks</li> <li>• Fluid retention may require intervention</li> <li>• Decreased sperm count</li> </ul>	<ul style="list-style-type: none"> <li>• Boxed warning: Fetal harm if taken during pregnancy, elevations of LFTs</li> <li>• Hypersensitivity to ambrisentan</li> </ul>	<ul style="list-style-type: none"> <li>• Unknown. Substrate of cytochrome P450 (CYP450) enzymes and P-glycoprotein (Pgp)</li> </ul>
<b>Epoprostenol</b>	Common: jaw pain, flushing, headache, myalgia, nausea and vomiting, hypotension, anxiety, chest pain, dizziness Serious: Sepsis	<ul style="list-style-type: none"> <li>• Abrupt withdrawal may result in rebound pulmonary hypertension</li> <li>• Requires close monitoring during dose initiation and dose adjustments</li> <li>• Concomitant bleeding risk factors, especially with anticoagulation therapy</li> <li>• Sepsis, related to drug delivery system</li> </ul>	<ul style="list-style-type: none"> <li>• Congestive heart failure with severe left systolic dysfunction</li> <li>• Pulmonary edema during dose initiation</li> <li>• Hypersensitivity to prostanoids</li> </ul>	<ul style="list-style-type: none"> <li>• Vasodilators, antihypertensives, diuretics: increased reduction in blood pressure</li> </ul>
<b>Treprostinil (subcutaneous)</b>	Common: infusion site pain, headache, diarrhea, nausea, jaw pain, dizziness, edema, pruritis, and hypotension	<ul style="list-style-type: none"> <li>• Abrupt withdrawal may cause rebound pulmonary hypertension</li> <li>• Increased risk of adverse effects in hepatic insufficiency</li> </ul>	<ul style="list-style-type: none"> <li>• None</li> </ul>	<ul style="list-style-type: none"> <li>• Diuretics, antihypertensives, or vasodilators: increased reduction in blood pressure</li> <li>• Anticoagulants: increased bleeding risk</li> </ul>
<b>Treprostinil (inhalation)</b>	Common: Cough, headache, nausea, dizziness, flushing, throat irritation, pharyngolaryngeal pain, and diarrhea	<ul style="list-style-type: none"> <li>• Safety and efficacy have not been established in patients with significant underlying lung disease</li> <li>• Symptomatic hypotension</li> <li>• Increased risk of bleeding</li> <li>• Concurrent CYP2C8 inhibitors or inducers</li> <li>• Hepatic or renal insufficiency may increase exposure and decrease tolerability</li> </ul>	<ul style="list-style-type: none"> <li>• None</li> </ul>	<ul style="list-style-type: none"> <li>• Diuretics, antihypertensives or other vasodilators: increased reduction in blood pressure</li> </ul>

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<b>Iloprost</b>	<p>Common: flushing, cough, headache, trismus, insomnia, back pain, nausea and vomiting          Serious: hypotension</p>	<ul style="list-style-type: none"> <li>• Hypotension (should not be initiated in patients with systolic blood pressure &lt; 85 mmHg)</li> <li>• Pulmonary edema when starting therapy</li> <li>• Avoid contact with skin or eyes</li> <li>• Bronchospasm in patients with hyperreactive airways</li> </ul>	<ul style="list-style-type: none"> <li>• None</li> </ul>	<ul style="list-style-type: none"> <li>• Anticoagulants: increased risk of bleeding</li> <li>• Antihypertensives and vasodilators: increase hypotensive effect</li> </ul>
<b>Tadalafil</b>	<p>Common: Headache, myalgia, dyspepsia          Serious: Hypotension, vision loss, hearing loss, priapism</p>	<ul style="list-style-type: none"> <li>• Cardiovascular disease and hypertension (not recommended in patients with pulmonary veno-occlusive disease)</li> <li>• Concomitant alpha-blockers or alcohol</li> <li>• Loss of vision</li> <li>• Hearing impairment</li> <li>• Combination with other PDE5 inhibitors</li> <li>• Prolonged erection</li> </ul>	<ul style="list-style-type: none"> <li>• Concomitant nitrates</li> <li>• Hypersensitivity to tadalafil</li> </ul>	<ul style="list-style-type: none"> <li>• Nitrates: additive hypotension</li> <li>• CYP3A4 inhibitors increases sildenafil concentration</li> <li>• Other PDE5 inhibitors</li> <li>• Alpha blockers: additive hypotension</li> <li>• Alcohol: hypotension</li> </ul>
<b>Sildenafil</b>	<p>Common:          Epitaxis, headache, dyspepsia, flushing, insomnia, erythema, dyspnea, rhinitis          Serious:          Hypotension, vision loss, hearing loss, priapism</p>	<ul style="list-style-type: none"> <li>• Cardiovascular disease and resting hypotension (not recommended in patients with pulmonary veno-occlusive disease)</li> <li>• Epitaxis in PAH secondary to connective tissue disease</li> <li>• Loss of vision</li> <li>• Hearing impairment</li> <li>• Combination with other PDE5 inhibitors</li> <li>• Prolonged erection</li> </ul>	<ul style="list-style-type: none"> <li>• Concurrent use of nitrates</li> <li>• Hypersensitivity to sildenafil</li> </ul>	<ul style="list-style-type: none"> <li>• Nitrates: additive hypotension</li> <li>• CYP3A4 inhibitors increases sildenafil concentration</li> <li>• Other PDE5 inhibitors</li> <li>• Alpha blockers</li> </ul>

LFT: liver function tests

PDE5: phosphodiesterase type 5