Producing smooth muscle relaxation and inflow of blood to the corpus cavernosum, Avanafil enhances the effect of NO by inhibiting phosphodiesterase type 5 (PDE-5), which is responsible for degradation of cGMP in the corpus cavernosum; when sexual stimulation causes local release of NO, inhibition of PDE-5 by avanafil causes increased levels of cGMP in the corpus cavernosum, resulting in smooth muscle relaxation and inflow of blood to the corpus cavernosum.

Dosage

Adult Erectile dysfunction: Oral: Initial: 100 mg taken ~15 minutes prior to sexual activity; taken as one single dose and not more than once daily; dose may be increased to 200 mg ~15 minutes prior to sexual activity or decreased to 50 mg ~30 minutes prior to sexual activity using the lowest dose that provides benefit; maximum 200 mg daily.

Dosing adjustment with concomitant medications: Alpha-blocker (dose should be stable at time of avanafil initiation): Initial avanafil dose: 50 mg taken as one single dose once and not more than once daily.

Moderate CYP3A4 inhibitors (including ampicillin, aprafen, aprepitant, diltiazem, erythromycin, foscarnet, fosamprenavir, verapamil): Maximum avanafil dose: 50 mg taken as one single dose and not more than once daily.

Strong CYP3A4 inhibitors (including atazanavir, clarithromycin, indinavir, lopinavir/ritonavir, ritonavir, telithromycin): Avoid concomitant use of avanafil.

Geriatric Elderly ≥65 years: Refer to adult dosing.

Renal Impairment: Adult

CCI ≥33 mL/min: Dose adjustment necessary. CCI <30 mL/Min: Has not been studied; use is not recommended by the manufacturer.

ESRF: Requires hemodialysis. Has not been studied; use is not recommended by the manufacturer.

Hepatic Impairment: Adult

Mild-to-moderate hepatic impairment (Child-Pugh class A or B): No dosage adjustment necessary.

Severe hepatic impairment (Child-Pugh class C): Has not been studied; use is not recommended by the manufacturer.

Administration: Adult

May be administered with or without food, ~15 to 30 minutes prior to sexual activity. Monitoring Parameters: Monitor for response, adverse reactions, blood pressure, and heart rate.

Drug Interactions

Avoid concomitant use of Avapritinib with any of the following: Thalidomide; Zolpidem

Prescribing and Access Restrictions Avapritinib is available in a select network of specialty pharmacies. For more information, refer to https://ayvakit.com/hcp.

Contraindications There are no contraindications listed in the manufacturer’s labeling.

Warnings/Precautions Intracranial hemorrhage, including subdural hematoma and cerebral hemorrhage, has been reported. Onset of intracranial hemorrhage ranged from ≤1 day to ≥2 years post-avapritinib initiation. Withhold avapritinib if intracranial hemorrhage develops and resume at a reduced dose after resolution, or permanently discontinue based on toxicity severity. CNS effects commonly included confusion, cognitive impairment, dizziness, sleep disorders, mood disorders, and hallucinations. Some events were severe (grade 3 or 4). The maximum number of CNS effects was ~15 weeks (range: 1 day to ≥2 years). CNS effects may require therapy interruption, dose reduction, and/or permanent discontinuation (based on severity of the toxicity).

Nausea, vomiting, and diarrhea were commonly reported, including cognitive impairment, dizziness, drowsiness, dysphoria, encephalopathy, fatigue, hallucination, headache, intracranial hemorrhage, irritability, mood disorder, personality changes, retrograde amnesia, sleep disorder, speech disturbance, and suicide attempt.

Dermatologic: Alopecia, hair discoloration, palm-plantar erythrodysesthesia, skin rash

Endocrine & metabolic: Ageusia, decreased serum albumin, decreased serum magnesium, decreased serum phosphorus, decreased serum potassium, decreased serum sodium, dysgeusia, hyperthyroidism, hypothyroidism, thyrotoxicosis, weight loss

Gastrointestinal: Abdominal pain, constipation, decreased appetite, diarrhea, dyspepsia, gastrointestinal hemorrhage, nausea, severe abdominal pain, severe vomiting, weight loss

Genitourinary: Testicular swelling

Hematologic & oncologic: Anemia, decreased serum albumin, decreased serum magnesium, decreased serum phosphorus, decreased serum potassium, decreased serum sodium, dysgeusia, hyperthyroidism, hypothyroidism, thyrotoxicosis, weight loss

Infection: Sepsis

Neuromuscular & skeletal: Ataxia

Ophthalmic: Increased lacrimation, ocular edema, pharyngeal edema, pleural effusion

Respiratory, thoracic: Dyspnea, pneumonia

Cardiovascular: Edema, facial edema, hypertension, peripheral edema, subdural hematoma

Central nervous system: Amnesia, anxiety, central nervous system toxicity, cerebral hemorrhage, cognitive dysfunction, dementia, disturbance in attention, dizziness, drowsiness, dysphoria, encephalopathy, fatigue, hallucination, headache, intracranial hemorrhage, irritability, mood disorder, personality changes, retrograde amnesia, sleep disorder, speech disturbance, suicidal ideation

Drug Interactions Metabolism/Transport Substrates of CYP2C9 (Major), CYP3A4 (Major); Note: Assignment of Major/Minor substrate status based on clinically relevant drug interaction potential

Avanafil is a substrate of CYP3A4.

Drug Interactions:

- With CYP3A4 (Major) inhibitors and inducers: Use caution.
- With Class Ia or Ic antiarrhythmics: Use caution.
- With CYP3A4 substrates: Use caution.
- With Class III antiarrhythmics: Use caution.
- With CYP3A4 inhibitors: Use caution.
- With CYP3A4 substrates: Use caution.

Brand Names: US: Avyklt

Drug Interactions:

- Avoid concomitant use of Avapritinib with any of the following:
  - Thalidomide; Zolpidem
  - Alcohol
  - Concomitant use of Avapritinib with any of the following:
  - Alcohol
  - Concomitant use of Avapritinib with any of the following:
  - Alcohol
  - Concomitant use of Avapritinib with any of the following:
  - Alcohol
  - Concomitant use of Avapritinib with any of the following:
  - Alcohol
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Prescribing and Access Restrictions Avapritinib is available in a select network of specialty pharmacies. For more information, refer to https://ayvakit.com/hcp.

Contraindications There are no contraindications listed in the manufacturer’s labeling.

Warnings/Precautions Intracranial hemorrhage, includ-
**Dosing**

**Pharmacodynamics/Kinetics**

Avapritinib is a potent tyrosine kinase inhibitor that blocks PDGFRα and PDGFRα D842 mutants, as well as KIT exon 11, 11/17, and 17 mutants. Certain PDGFRα and KIT mutations may result in autophosphorylation and constitutive activation of these receptors, which can contribute to tumor cell proliferation. Avapritinib inhibits autophosphorylation of Kit D816V and PDGFRα D842V, which are mutants associated with resistance to approved kinase inhibitors.

**Dosage Forms:** US

- Oral: Avapro, Avapro HCT, Avapro-e, AVAR-e, AVAR-LS
- Intravenous: Avapro IV
- Powder for Oral/Parenteral Administration: AVATROMBOPAG

**Monitoring Parameters**

**Dosage adjustment for concomitant therapy:**

- CYP2C9 inducers: Avoid concomitant use with moderate or strong CYP3A inhibitors. If coadministration with a moderate CYP3A inhibitor cannot be avoided, reduce dose to 100 mg once daily.
- CYP3A inducers: Avoid concomitant use with moderate or strong CYP3A4 inducers.

**Renal Impairment:**

**Note:** Renal function evaluated by Cockcroft-Gault equation.

<table>
<thead>
<tr>
<th>ClCr (mL/min)</th>
<th>Dose adjustment</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 to 29</td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>30 to 59</td>
<td>Reduce dose to 100 mg once daily</td>
</tr>
<tr>
<td>60 to 89</td>
<td>Reduce dose to 50 mg once daily</td>
</tr>
<tr>
<td>90 to 120</td>
<td>Reduce dose to 25 mg once daily</td>
</tr>
<tr>
<td>&gt;120</td>
<td>No dose adjustment necessary</td>
</tr>
</tbody>
</table>

**Hepatic Impairment:**

**Adult**

Mild (total bilirubin ≤ ULN and AST > ULN or total bilirubin 1 to 1.5 times ULN and any AST) or moderate (total bilirubin >1.5 to 3 times ULN and any AST) impairment: No dose adjustment necessary.

Severe impairment (total bilirubin >3 times ULN and any AST): There are no dosage adjustments provided in the manufacturer's labeling.

Other considerations:

- **Severe:** Avoid concomitant use with moderate or strong CYP3A4 inhibitors.
- **Mild:** Avoid concomitant use with moderate or strong CYP3A4 inducers.

**CNS effects:**

- Grade 1: Continue avapritinib at the same dose or withheld avapritinib until improvement to baseline or resolution; resume at the same or reduced dose.
- Grade 2 or 3: Withhold avapritinib until improvement to baseline, grade 1, or resolution; resume at the same or reduced dose.
- Grade 4: Permanently discontinue avapritinib.

**Contraindications:**

-*Trombopag* is present in breast milk. Due to the potential for tumor cells to proliferate, breastfeeding is contraindicated.

**Pregnancy Considerations:**

Based on findings from animal reproduction studies, in utero exposure to avatrombopag may cause fetal harm. Breastfeeding Considerations: It is not known if avatrombopag is present in breast milk. Due to the potential for tumor cells to proliferate, breastfeeding is contraindicated.