Health Alliance: Nexavar® (sorafenib)

PROGRAM RATIONALE
Client Requested: The intent of the criteria is to ensure that patients follow selection elements established by Health Alliance medical policy for Nexavar.

FDA-APPROVED INDICATIONS
Nexavar is indicated for the treatment of patients with:
- Advanced renal cell carcinoma (RCC)\textsuperscript{1-4}
- Unresectable hepatocellular carcinoma (HCC)\textsuperscript{1-3}

Compendial Uses
Thyroid carcinoma\textsuperscript{2,3}
- Follicular, papillary, or Hürthle cell thyroid carcinoma: treatment of clinically progressive or symptomatic metastatic disease in patients with nonradioiodine-responsive tumors at sites other than central nervous system
- Medullary thyroid carcinoma: treatment of disseminated symptomatic disease if clinical trials or vandetanib are not available or appropriate, or if there is progression on vandetanib

Soft tissue sarcoma\textsuperscript{2}
- Gastrointestinal stromal tumor (GIST): treatment of progressive disease when the patient is no longer receiving benefit from imatinib or sunitinib
- Angiosarcoma as a single agent
- Desmoid tumors (aggressive fibromatosis): initial treatment or treatment of recurrence for gross residual disease following surgery, for unresectable disease, or for disease for which surgery would be unacceptably morbid

CLINICAL BACKGROUND
The intent of the criteria is to ensure that patients follow selection elements noted in labeling. Nexavar is indicated for the treatment of patients with advanced RCC and unresectable HCC.\textsuperscript{1-4} Compendial uses include 1) treatment of follicular, Hürthle cell, papillary, or medullary thyroid carcinoma, 2) treatment of progressive GIST, 3) treatment of angiosarcoma and 4) treatment of desmoid tumors.\textsuperscript{2,3}

Nexavar is a kinase inhibitor that inhibits multiple intracellular (CRAF, BRAF and mutant BRAF) and cell surface kinases (KIT, FLT-3, RET, VEGFR-1, VEGFR-2, VEGFR-3, and PDGFR-β).\textsuperscript{1} Inhibition of these kinases with sorafenib results in a reduction in tumor growth and angiogenesis.

SAFETY
Nexavar in combination with carboplatin and paclitaxel is contraindicated in patients with squamous cell lung cancer.\textsuperscript{1} A randomized controlled trial compared Nexavar versus placebo in patients receiving carboplatin and paclitaxel for non-small cell lung cancer.\textsuperscript{1} The study was stopped early because overall survival was not improved with Nexavar. In a subset of patients with squamous cell carcinoma, higher mortality was observed in patients who received Nexavar (in combination with carboplatin and paclitaxel).\textsuperscript{1}

In RCC and HCC clinical trials, the incidence of cardiac ischemia or infarction was higher in the Nexavar groups than in the placebo groups.\textsuperscript{1} Temporary or permanent discontinuation of Nexavar should be considered in patients who develop cardiac ischemia or infarction. An increased risk of bleeding may occur after administration of Nexavar. If any bleeding necessitates medical intervention, permanent discontinuation of Nexavar should be considered. Nexavar can prolong the QT/QTc interval which increases the risk for ventricular arrhythmias. Avoid Nexavar in patients with congenital long QT syndrome.

Hypertension has been reported in pivotal trials of Nexavar in patients with HCC or RCC.\textsuperscript{1} Hypertension was usually mild to moderate, occurred early in the course of treatment, and was managed with standard antihypertensive therapy. In cases of severe or persistent hypertension, despite use of antihypertensive therapy, temporary or permanent
discontinuation of Nexavar should be considered. Blood pressure should be monitored weekly during the first six weeks of Nexavar therapy and thereafter monitored and treated in accordance with standard medical practice.

Hand-foot skin reaction and rash represent the most common adverse reactions attributed to Nexavar. Management of dermatologic toxicities may include topical therapies for symptomatic relief, temporary treatment interruption, and/or dose modification of Nexavar, or in severe or persistent cases, permanent discontinuation of Nexavar.

**NEXAVAR ALGORITHM**

**ABBREVIATIONS**
GIST = gastrointestinal stromal tumors  
HCC = hepatocellular carcinoma  
RCC = renal cell carcinoma.
REFERENCES

DOCUMENT HISTORY
Written: Specialty Clinical Development (WH) 04/2013
Revised:
Reviewed: CDPR/SES 04/2013

The Participating Group signed below hereby accepts and adopts as its own the criteria for use with Specialty Guideline Management, as administered by CVS Caremark.

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Signature                                              Date

Client Name