CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-290

OFFICE DIRECTOR MEMO

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NDA: 22-290

DRUG: Iobenguane I-123 injection (AdreView)

ROUTE: intravenous administration as an injection over 1 to 2 minutes

INDICATION: AdreView is a radiopharmaceutical indicted for the use in the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests.

RECOMMENDED REGULATORY ACTION: Approval

Iobenguane I 123 (AdreView, GE Healthcare) is a diagnostic radiopharmaceutical, for use in the detection of primary or metastatic pheochromocytoma or neuroblastoma as an adjunct to other diagnostic tests. Iobenguane accumulates in adrenergically innervated tissues as well as tumors derived from the neural crest. The uptake of iobenguane I by metabolically active pheochromocytoma or neuroblastoma allows scintigraphic visualization of these tumors.

The safety and efficacy of iobenguane I 123 were evaluated in a single arm clinical study of patients with known or suspected neuroblastoma or pheochromocytoma. Diagnostic efficacy was determined for 211 patients by comparison of focal increased radionuclide uptake on planar scintigraphy at 24 ± 6 hours post-administration of iobenguane I 123 against the definitive diagnosis (standard of truth). The standard of truth was a diagnosis of pheochromocytoma in 127 of the patients and neuroblastoma in 84 patients. The standard of truth for the presence or absence of metabolically active pheochromocytoma or neuroblastoma was determined by histopathology or, when histopathology was

unavailable, a composite of imaging, plasma/urine catecholamine and/or catecholamine metabolite measurements, and clinical follow-up. In the detection of either neuroblastoma or pheochromocytoma, the iobenguane I 123 sensitivity and specificity were determined independently by three readers who were fully masked to clinical information. The average sensitivity ranged from approximately 77% to 80% and the specificity ranged from 69% to 77%. Performance characteristics were similar between the groups of patients who had either a pheochromocytoma or neuroblastoma truth standard.

The AdreView performance characteristics (sensitivity and specificity) did not meet the statistically-predefined limits for success. The predefined statistical criteria were based upon published literature. The published literature may be biased toward over estimation of the performance characteristics of I-123 iobenguane sulfate. The image interpretations are performed with knowledge of clinical data. This study conducted by GE Healthcare excluded all clinical data from image interpretation. The sensitivity from the study of AdreView was approximately 80% and the specificity was 75%; these outcomes are clinically solid evidence of acceptable diagnostic performance since the study used extremely rigorous methods in image interpretation. Performance characteristics are similar to those for the I-131 form of iobenguane sulfate.

AdreView presents no new safety findings beyond those typical for a radionuclide and, in comparison to the I-131 version of iobenguane sulfate, may offer safety advantages. No post-marketing committments or requirements are needed. During the 24 hours following iobenguane administration, adverse reactions were mild to moderate in severity and were predominantly isolated occurrences (≤ 2 patients) of one of the following reactions: dizziness, rash, pruritis, flushing or injection site hemorrhage. No serious adverse reactions were reported.

The recommended dose of iobenguane I 123 is 10 mCi (370 mBq) for patients ≥ 16 years of age or patients < 16 years of age who weigh ≥ 70 kg. The dose for patients < 16 years of age who weigh < 70 kg is based upon a scale described in the product insert.

Iobenguane Sulfate I-131, manufactured and marketed by CIS-US is a related drug. This product is the I-131 form of iobenguane and is indicated "as an adjunctive diagnostic agent in the localization of primary or metastatic pheochromocytomas and neuroblastomas." The I-131 in this product is both a beta particle and a gamma ray emitter. In contrast, I-123 is only a gamma ray emitter. The I-123 form of iobenguane sulfate is currently used because of the perceived "improved image quality" of this radio-imaging agent, compared to the I-131 marketed product. The I-123 iobenguane used in current clinical practice is manufactured in compounding pharmacies or at local facilities.

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/s/

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