Division of Hepatology and Nutrition

REGULATORY PROJECT MANAGER AND CLINICAL LABELING REVIEW

Applications:

Application	Supplement	Product Name	Date of Receipt of Original Submission	Date of Receipt of the Resubmission
NDA 209379	S-004	Selenious Acid Injection, USP	5/14/2020	4/30/2021

Applicant: American Regent, Inc.

Labeling Reviewed

Material	**Submit Date**	**Receipt Date**	**Compared to**
Prescribing Information (PI)	5/14/2020	5/14/2020	7/2019 last approved PI

Background and Summary Description

This Prior Approval supplemental new drug application provides for the response to the Complete Response Letter dated November 6, 2021 for the following:

- the addition of a new strength, 12 mcg/2 mL (6 mcg/mL), and
- the commitment to fulfill the Pediatric Research Equity Act (PREA), post-marketing requirement (PMR) 3613-1: Develop an age-appropriate formulation to ensure accurate dosing by volume for pediatric patients weighing less than 7 kg.

Review

Recommendations based on the addition of the new strength, 6 mcg/mL, are as follows:

- **2.5 Recommended Dosage in Adults and Pediatric Patients**
  - There are two dosage strengths for Selenious Acid Injection: 6 mcg/mL and 60 mcg/mL of selenium.
  - Selenious Acid Injection in a concentration of 6 mcg/mL is recommended for use in pediatric patients, particularly those weighing 7 kg or less.

- **3 DOSAGE FORMS AND STRENGTHS**

    - Single-dose Vial: 12 mcg/2 mL (6 mcg/mL) of selenium
- **11 DESCRIPTION**
    - Each 6 mcg/ml single-dose vial contains 2 mL of selenious acid solution.
    - None of the presentations contain preservatives.
    - Each mL of the 60 mcg/mL strength contains 60 mcg of selenium present as 98 mcg of selenious acid, nitric acid for pH adjustment (1.8 to 2.4), and water for injection q.s.
    - Each mL of the 6 mcg/mL strength contains 6 mcg of selenium present as 9.8 mcg of selenious acid, nitric acid for pH adjustment (1.8 to 2.4), and water for injection q.s.
- **16 HOW SUPPLIED/STORAGE AND HANDLING**
    - 12 mcg/2 mL (6 mcg/mL) of selenium in a 2 mL single-dose vial. Carton of 10 vials (NDC 0517-6502-10).

Reviewer Comments: The proposed changes above are acceptable.

The DMEPA team review dated 7/27/2020 in DARRTS found that the labeling revisions (PI, Carton & Container) are acceptable from a medication error perspective.

A consultation conducted by Dr. An Massaro of the Office of Pediatric Therapeutics (OPT) and dated 8/5/2021 recommended that the following be added to Section "2.6 Recommended Dosage in Adults and Pediatric Patients" under "Monitor selenium concentrations during treatment":

> Plasma selenium concentrations in healthy infants and children have been reported to range 5 to 15 µg/L, with lower levels (1.6-13.4 µg/L) reported in preterm infants.

During internal DHN discussion of the OPT recommendation, a decision was made that rather than add a selenium concentration reference range for pediatric patients, that we would remove the statement shown below about the adult reference range. The rationale was that the reference ranges, as stated in labeling, may vary based on the assay used. The OPT team agreed to this removal of the adult reference range in place of adding the pediatric reference range.

Table 1: Recommended Dosage of Selenious Acid Injection for Adults and Pediatric Patients by Estimated Weight

Population	Recommended Dosage
Adults	60 mcg/day
Pediatric Patients 7 kg and above	2 mcg/kg/day (up to 60 mcg/day)
Pediatric Patients less than 7 kg	2 to 4 mcg/kg/day

- Monitor selenium concentrations during treatment. Selenium concentrations may vary depending on the assay used and the laboratory reference range. ~~The lower end of the range reported in healthy adults is 7 to 10 mcg/dL.~~

PREA PMR

Per the Sponsor's general correspondence received on September 10, 2020, the addition of a new strength, 6 mcg/mL is to fulfill the postmarketing requirement under Pediatric Research Equity Act (PREA) for the following PMR:

3613-1: Develop an age-appropriate formulation to ensure accurate dosing by volume for pediatric patients weighing less than 7 kg.

Final Report Submission: 08/2020

Therefore, a PeRC meeting was scheduled on September 29, 2020, and PeRC concurred with the Division's assessment that the new strength fulfilled the above PREA PMR.

Therefore, the PI was revised to the reflect the above changes and was sent to the Applicant on July 27, 2021 and August 5, 2021 and received on July 29, 2021 and August 6, 2021, respectively.

Prescribing Information

The version of the PI submitted on August 6, 2021 is considered to be final.

Recommendation(s)

This supplement is recommended for approval.

Reviewers

Thao Vu, R.Ph., Regulatory Project Manager, DHN
Judy Racoosin, M.D., M.P.H., Deputy Director, Safety, DHN

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

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