Title: EVENITY® Risk Minimisation Materials Effectiveness Measurement in Australia

Amgen Protocol Number: 20220120

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Therapeutic Area:	Bone/Endocrinology
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1. BACKGROUND AND RATIONALE

EVENITY® (romosozumab) is a humanized immunoglobulin G2 monoclonal antibody with high affinity and specificity for sclerostin. It is indicated for the treatment of osteoporosis in postmenopausal women at high risk of fracture. EVENITY is also indicated for treatment to increase bone mass in men with osteoporosis at high risk of fracture.

To support the safe use of EVENITY, Amgen developed educational materials (aRMMs) for Endocrinologists, Rheumatologists, Geriatricians, General Physicians, patients and their caregivers to address the cardiovascular risks associated with EVENITY. These risks include:

- Myocardial infarction (MI)
- Stroke

Amgen Australia is required by the Therapeutics Goods Administration (TGA) to assess the effectiveness of the educational materials in addressing the cardiovascular risks in patients prescribed EVENITY following implementation in Australia.

1.1 Educational Materials

Amgen provides the following educational materials to healthcare providers (Specialists) who can prescribe EVENITY:

- Prescriber guide
- Patient alert card (included in the Patient Booklet)

2. OBJECTIVES

The objective of this study is to measure the effectiveness of the educational materials (prescriber guide and patient alert card) on awareness, utilization and adequacy targeted to Endocrinologists, Rheumatologists, Geriatricians and General Physicians in addressing the cardiovascular risks (myocardial infarction and stroke) associated with the use of EVENITY.

2.1 Primary

There are three key research objectives:

- Measure awareness of the educational materials amongst Specialists (Endocrinologists, Rheumatologists, Geriatricians and General Physicians)
- Identify if Specialists distribute the educational materials to their patients and/or caregivers when prescribing EVENITY
- Determine adequacy of the content of the education materials to support Specialists in prescribing EVENITY to patients.

3. STUDY POPULATION/SAMPLE SIZE/STATISTICAL ANALYSES PLANS

A market research vendor will be contracted to conduct a survey to assess the effectiveness of the educational materials provided to Specialists. This survey will consist of a questionnaire targeted to Endocrinologists, Rheumatologists, Geriatricians and General Physicians in Australia who can prescribe EVENITY to patients. The content of the questionnaire will be developed with an experienced vendor in collaboration with medical, commercial, drug safety and regulatory staff from Amgen. As per the Australian Specific Annex (ASA) provided to the TGA, specific questions will be included to assess:

- Awareness of the aRMMs
- Utilisation of the aRMMs
- Adequacy of the aRMMs in addressing the cardiovascular risk

Only Specialists who can prescribe EVENITY to patients will be selected to participate in the survey. Participants will be selected from the Amgen Australia approved contact lists of Specialists who can prescribe EVENITY and other osteoporosis treatments with relevant consent. All participants will be required to complete the study research informed consent form.

Recruitment will be undertaken by the experienced vendor and will be on a best endeavours basis with follow-up. The research vendor team will contact relevant Specialists and send a link to the survey component of the study for the participant to complete when convenient. The vendor will contact recipients of the survey at least five times (3 emails or faxes and 2 phone calls) throughout the fielding stage to encourage completion of the questionnaire. The fielding stage is expected to occur over at least a 4 week period.

Survey participation is voluntary and is conducted under the Australian Market Research guidelines. Participants who complete the survey will be compensated for their participation at rates within the standard fair market values required by Amgen compliance and Australian Market Research guidelines. Estimated honoraria is:

- AUD $[redacted] per completed survey

Survey participant details are confidential and are not provided to Amgen by the vendor. Questionnaire results provided to Amgen will be data tables of the responses captured with no participant identifiers.

The survey will be conducted in Q1 2023.

The vendor will provide aggregated survey data and a descriptive report of the methodology. The descriptive report will include:

- Study methodology
- Study sampling, including a breakdown of the number of Specialists invited to participate in the survey, the number of respondents who were eligible and the number who completed the survey
- Final participation rate
- Tabulated results

Survey brief is included in Appendix 1.

Survey draft questionnaire is included in Appendix 2.

The aRMMs will be considered effective based on awareness, utilization and adequacy if ≥80% positive response rate is achieved from respondents based on overall score of questions assessing:

  - Awareness of the aRMMs (refer to main survey questions Q01, Q2, Q5 and Q06)
  - Utilisation of the aRMMs (refer to main survey questions Q03, Q04, Q7 and Q8)
  - Adequacy of the aRMMs in addressing the cardiovascular risk (refer to main survey questions Q09 and Q10)

The metric for the measure of success has been selected as this was considered an acceptable response rate by the TGA for a similar project conducted assessing the effectiveness of risk minimisation materials for Amgen products CCI [redacted]

Refer to Table 1 for itemisation of positive and negative survey responses.

Table 1. Itemisation of Positive and Negative Survey Responses

Question No.	Positive Response	Negative Response
Q1. Awareness of aRMMs	Yes – Description of Prescriber guide and/or Patient alert card	No or none
Q2. Awareness of aRMMs	1 and/or 2	3
Q3. Utilisation of aRMMs	1	2
Q4. Utilisation of aRMMs	Response unrelated to aRMMs	Response related to aRMMs
05. Awareness of aRMMs	Able to recall Safety risk(s)	Unable to recall Safety risk(s)
06. Awareness of aRMMs	4	1, 2, 3 or 5
07. Utilisation of aRMMs	1 or 2	3 or 4
08. Utilisation of aRMMs	Response related to 1 or 2 from Q07	Response related to 3 or 4 from Q07
09. Adequacy of aRMMs	Overall score of Strongly agree or Somewhat agree	Overall score of Strongly disagree or Somewhat disagree
10. Adequacy of aRMMs	None or response related to aRMMs adequately addressing CV risk	Response related to aRMMs not adequately addressing CV risk

3.1 Limitations of the Research Methods

The sample size will be 765 Specialists (based on aRMMs distribution list). Target number of responses is between 30-50 based on vendor expertise. It will be challenging to achieve a target of n=50 complete survey responses due to potential non-participation or low response rate and selective nature of respondents.

4. COLLECTION, RECORDING, AND REPORTING OF SAFETY INFORMATION AND PRODUCT COMPLAINTS

4.1 Definition of Reportable Events

4.1.1 Adverse Events

An adverse event is any untoward medical occurrence in a patient administered a pharmaceutical product(s) irrespective of a causal relationship with this treatment.

An adverse event can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated

with the use of a product(s), whether or not considered related to the product(s). The definition of an adverse event includes:

- Worsening of a pre-existing condition or underlying disease
- Events associated with the discontinuation of the use of a product(s), (eg, appearance of new symptoms)

4.1.2 Serious Adverse Events

A serious adverse event is any adverse event as defined above that meets at least one of the following serious criteria:

- is fatal
- is life threatening (places the patient at immediate risk of death)
- requires in-patient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity
- is a congenital anomaly/birth defect
- is an “other medically important serious event” that does not meet any of the above criteria

A hospitalization meeting the regulatory definition for “serious” is any in-patient hospital admission that includes a minimum of an overnight stay in a healthcare facility.

“Other medically important serious events” refer to important medical events that may not be immediately life threatening or result in death or hospitalization but may jeopardize the patient or may require intervention to prevent one of the other outcomes listed in the definition above. Examples of such events could include allergic bronchospasm, convulsions, and blood dyscrasias, drug-induced liver injury, events that necessitate an emergency room visit, outpatient surgery, or other events that require other urgent intervention.

4.1.3 Other Safety Findings

Other Safety Findings (regardless of association with an adverse event) include:

- Medication errors, overdose/underdose, whether accidental or intentional, misuse, addiction, or abuse involving an Amgen product,
- Use of an Amgen product while pregnant and/or breast feeding,
- Transmission of infectious agents,
- Reports of uses outside the terms for authorized use of the product including off-label use,
- Accidental or Occupational exposure,
- Any lack or loss of intended effect of the product(s).

4.1.4 Product Complaints

Product Complaints include any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a drug, combination product, or device after it is released for distribution to market or clinic. This includes any drug(s), device(s) or combination products provisioned and/or repackaged/modified by Amgen. Drug(s) or device(s) or combination product(s) includes investigational product.

4.2 Safety Collection, Recording and Submission to Amgen Requirements

4.2.1 Prospective Data Collection

The 20220120 study is collecting information from healthcare professionals, at a point in time via a market research project utilizing a targeted questionnaire. Safety collection and recording requirements are conducted in accordance with the Amgen Market Research safety reporting requirements.

Project Name: Project Soteria

Protocol Number: 22-00410

5. Research Agency: Hummingbird InsightSUBJECT CONFIDENTIALITY

This study will comply with all applicable laws regarding subject privacy. No direct subject contact or collection of additional subject data will occur. Study results will be in tabular form and aggregate analyses that omits subject identification. Any reports will not include subject identifiers.

6. PUBLICATION INTENT

There is no intent to publish the results of this study.

7. APPENDICES

7.1 Appendix 1: Study Research Brief

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7.2 Appendix 2: Study Research Survey

EVENITY aRMMs Questionnaire

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