

**OPINION ON
MEDICINAL
PRODUCTS****regadenoson**
RAPISCAN 400 µg,
solution for injection
New indication**Adopted by the Transparency Committee on 18 January 2023****SUMMARY****The legally binding text is the original French opinion version****Key points**

Approval of reimbursement of RAPISCAN (regadenoson) as pharmacological stress agent for myocardial perfusion imaging in adult patients unable to undergo adequate exercise stress.

The Committee points out the need for procedures associated with RAPISCAN (regadenoson) (myocardial perfusion positron emission tomography [PET] and perfusion coronary computed tomography [CT]) to be assessed with a view to funding.

Therapeutic improvement?

No therapeutic improvement in the diagnostic management of myocardial ischemia by pharmacological stress perfusion imaging in patients unable to undergo adequate exercise stress.

Role in therapeutic strategy?

The diagnostic management and assessment of chronic coronary syndrome, which requires exploring the adaptability of coronary circulation during stress, is the subject of a care pathway guide prepared by HAS and published in 2021, and *European Society of Cardiology* (ESC) guidelines published in 2019 are also available.

The first stage of the care pathway is based on the clinical examination, which the clinician uses as a basis to calculate the pre-test probability (PTP) using validated scores. It involves estimating the probability of having obstructive coronary disease which will then determine the nature of the investigations to be carried out where applicable.

Best practice guidelines recommend the use of non-invasive imaging tests as first-line tests for intermediate- and high-PTP patients. The objective is to reserve coronary angiography, which is an invasive test, for patients who absolutely need it (with a view to possible coronary revascularisation). It is recommended to select the initial non-invasive diagnostic test according to the clinical probability of obstructive coronary disease and other patient characteristics influencing test performance, patient preferences, local expertise, and test availability.

For patients for whom coronary disease cannot be ruled out by clinical assessment alone, non-invasive diagnostic tests (coronary CT or non-invasive functional imaging tests) are recommended as a first-line approach, while exercise stress tends to be recommended as a second-line approach where other non-invasive or invasive imaging methods are not available:

- coronary CT, due to its ability to rule out disease, is the preferred test in cases of low or intermediate PTP of ischemic heart disease (< 15%) in patients allowing good image acquisition (no calcification, obesity, arrhythmia, etc.) and with no history of ischemic heart disease;
- functional tests coupled with non-invasive imaging have a benefit in the detection and quantification of ischemic heart disease, and in the assessment of myocardial viability with a view to revascularisation; therefore, they should be preferred for patients with an intermediate (PTP between 5 and 15%) or high (PTP > 15%) probability of ischemic heart disease to guide myocardial revascularisation;
- the role of exercise stress in the diagnostic strategy in respect of chronic coronary syndrome is different according to the guidelines:
 - the ESC does not recommend it as a first-line approach, but as an alternative test to confirm or rule out coronary disease where other non-invasive or invasive imaging methods are not available;
 - the French Society of Cardiology (SFC) recommends it as a first-line approach, specifying that its interpretation and benefit must not be confined to studying repolarisation alone.

For functional imaging stress tests (echocardiography, cardiac MRI, SPECT, PET), myocardial ischemia may be induced:

- by a stress test recommended as a first-line approach where the patient is capable of sufficient or optimal exercise (this physiological test enables better assessment of how the heart adapts to exercise);
- or by a pharmacological stimulation test if the stress test is not feasible: using a positive inotropic agent (dobutamine) or vasodilators (dipyridamole, adenosine, regadenoson).

It should be noted that besides echocardiography, dobutamine-induced pharmacological stress is very rarely used in routine practice, and national learned societies (French Society of Radiology

[SFR], French Society of Cardiovascular Imaging [SFICV] and French Society of Cardiology [SFC]) recommend preferential use of vasodilator agents for other myocardial perfusion imaging procedures.

Role of the medicinal product

RAPISCAN (regadenoson) is a diagnostic option in the same way as proprietary medicinal products based on adenosine and dipyridamole (although they are off-label apart from myocardial scintigraphy) for use as a pharmacological stress agent for myocardial perfusion imaging in adult patients unable to undergo adequate exercise stress.

Committee's conclusions

Clinical Benefit

- ➔ The severity of the condition is defined according to the results of the myocardial perfusion imaging investigation. The diseases screened with imaging tests requiring the use of RAPISCAN (regadenoson) can be serious diseases that are life-threatening and/or severely impair quality of life.
- ➔ The proprietary medicinal product RAPISCAN (regadenoson) is a diagnostic medicinal product.
- ➔ The efficacy/adverse effect ratio of RAPISCAN (regadenoson) is low, given the methodological weakness of the data and the associated adverse effects.
- ➔ Alternative medications are available in the form of other pharmacological stress agents, particularly adenosine and dipyridamole, although they are used off-label apart from for myocardial perfusion scintigraphy (SPECT).
- ➔ RAPISCAN (regadenoson) is a diagnostic option in the same way as proprietary medicinal products based on adenosine and dipyridamole (although they are off-label apart from myocardial scintigraphy scans) for use as a pharmacological stress agent for myocardial perfusion imaging in adult patients unable to undergo adequate exercise stress.

➔ Public health benefit

Considering:

- the severity and the high incidence of chronic coronary syndrome,
- the partially met medical need, but with a persistent need for authorised medicinal products for the different types of myocardial perfusion imaging tests that are effective, easy to administer and well-tolerated,
- the lack of response to the identified need on account of:
 - the lack of evidence of an impact on the treatment of coronary disease, particularly in terms of morbidity-mortality and quality of life,
 - the lack of evidence of any impact on delivery of care,

RAPISCAN (regadenoson) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the actual clinical benefit of RAPISCAN (regadenoson) is low as a selective coronary vasodilator intended for use in adults as a pharmacological stress agent for myocardial perfusion imaging (MPI) in adult patients unable to undergo adequate exercise stress.

The Committee approves inclusion in the list of proprietary medicinal products approved for community use as a selective coronary vasodilator for myocardial perfusion imaging (MPI) in adult patients unable to undergo adequate exercise stress and at the marketing authorisation dosages.

The Committee points out the need for procedures associated with RAPISCAN (regadenoson) (myocardial perfusion positron emission tomography [PET] and perfusion coronary computed tomography [CT]) to be assessed with a view to funding.

Clinical Added Value

Considering:

- the exploratory nature of the data furnished which suggest similar diagnostic performances between regadenoson and adenosine, but which do not fail to establish the diagnostic benefit of regadenoson;
- the lack of data in respect of the superiority of the efficacy of regadenoson with respect to adenosine or dipyridamole;
- an acceptable safety profile of regadenoson with however the potential onset of serious adverse effects particularly of a cardiovascular nature;
- the partially met medical need by adenosine and dipyridamole, although used off-label apart from for myocardial scintigraphy;

the Transparency Committee deems that RAPISCAN (regadenoson) provides no clinical added value (CAV V) in the diagnostic strategy of myocardial ischemia by pharmacological stress perfusion imaging among patients unable to undergo adequate exercise stress.

RAPISCAN 400 µg, 18 January 2023
All our publications can be found on www.has-sante.fr