Gemeinsamer Bundesausschuss

Justification

for the Resolution of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V
Colchicine (known active ingredient with new data protection: for the prevention of ischaemic cardiovascular events in patients with atherosclerotic CHD following a myocardial infarction)

From 20 August 2026

Contents

1. Legal basis

According to Section 35a paragraph 6 SGB V, the Federal Joint Committee (G-BA) can initiate a benefit assessment according to paragraph 1 for a medicinal product with an active ingredient that is not a new active ingredient according to Section 35a, paragraph 1, sentence 1 SGB V, if a new marketing authorisation with new dossier protection is granted for the medicinal product. According to Chapter 5 Section 16, paragraph 1, sentence 3 of the Rules of Procedure of the G-BA (VerfO), a benefit assessment according to Section 35a paragraph 6 SGB V can be initiated in particular for medicinal products whose therapeutic indication differs from the therapeutic indication of medicinal products with the same known active ingredients. According to Chapter 5 Section 16, paragraph 1, sentence 4 VerfO, a deviation may result in particular from changes in a therapeutic indication that are attributable to a different therapeutic indication compared to the therapeutic indication of the medicinal product with the same known active ingredient, by the fact that:

- the therapeutic indication relates to a different group of patients or
- the therapeutic area (treatment, diagnosis or prevention) differs.

The benefit assessment is carried out on the basis of evidence, which must be submitted to the G-BA electronically by the pharmaceutical company - including all clinical studies they have conducted or commissioned - at the latest at the time of the first placing on the market of the medicinal product. Their submission must include the following information in particular:

1. approved therapeutic indications,

2. medical benefit,

3rd additional medical benefit in relation to the appropriate comparator therapy,

4th number of patients and patient groups for whom there is a therapeutically significant additional benefit,

5th treatment costs for the statutory health insurance funds,

6th requirements for a quality-assured application.

The G-BA may commission the Institute for Quality and Efficiency in Health Care (IQWiG) to carry out the benefit assessment. According to Section 35a, paragraph 2 SGB V, the assessment must be completed within three months of the relevant date for submission of the evidence and published on the internet.

According to Section 35a paragraph 3 SGB V, the G-BA decide on the benefit assessment within three months of its publication. The resolution is to be published on the internet and is part of the Pharmaceuticals Directive.

2. Key points of the resolution

At their session on 17 July 2025, the G-BA decided to initiate a benefit assessment for the active ingredient colchicine in the indication "prevention of ischaemic cardiovascular events in adults with atherosclerotic coronary heart disease following a myocardial infarction"

according to Section 35a, paragraph 6 SGB V in conjunction with Chapter 5 Section 16, paragraph 1 VerfO.

The medicinal product Colxi, containing the active ingredient colchicine, was first placed on the market on 1 March 2026. Relevant date according to Chapter 5 Section 8, paragraph 1, number 7 VerfO for the start of the assessment procedure for the active ingredient colchicine is within three months of the request by the G-BA. If the medicinal product has not yet been placed on the market at that time, the procedure shall start on the date on which it is first placed on the market.

The final dossier was submitted to the G-BA in due time on 27 February 2026. The assessment procedure started on 1 March 2026.

The G-BA commissioned the IQWiG to carry out the assessment of the dossier. The benefit assessment was published on 1 June 2026 on the G-BA website at (www.g-ba.de), thus initiating the written statement procedure. In addition, an oral hearing was held.

The G-BA came to a resolution on whether an additional benefit of colchicine compared with the appropriate comparator therapy could be determined on the basis of the dossier of the pharmaceutical company, the dossier assessment prepared by the IQWiG, the statements submitted in the written statement and oral hearing procedure, and the addendum to the benefit assessment prepared by IQWiG. In order to determine the extent of the additional benefit, the G-BA have evaluated the data justifying the finding of an additional benefit on the basis of their therapeutic relevance (qualitative), in accordance with the criteria laid down in Chapter 5 Section 5, paragraph 7 VerfO. The methodology proposed by the IQWiG in accordance with the General Methods [1] was not used in the benefit assessment of colchicine.

In the light of the above, and taking into account the statements received and the oral hearing, the G-BA have made the following assessment:

2.1 Additional benefit of the medicinal product in relation to the appropriate comparator therapy

2.1.1 Approved therapeutic indication of colchicine (Colxi) in accordance with the product information

Adults

Prevention of ischaemic cardiovascular events in patients with atherosclerotic coronary heart disease and a recent myocardial infarction (MI), in addition to standard therapies.

Therapeutic indication of the resolution (resolution of 20.08.2026):

See the approved therapeutic indication

[1] General Methods, version 8.0 from 19.12.2025. Institute for Quality and Efficiency in Health Care (IQWiG), Cologne.

2.1.2 Appropriate comparator therapy

The appropriate comparator therapy was determined as follows:

Adults with atherosclerotic coronary heart disease and a recent myocardial infarction (MI) who are indicated for the prevention of ischaemic cardiovascular events

Appropriate comparator therapy:

- An optimised standard therapy for the secondary prevention of ischaemic cardiovascular events in patients with atherosclerotic coronary heart disease and a recent myocardial infarction (MI), as well as for the treatment of any existing concomitant diseases, e.g., hypertension, heart failure, diabetes mellitus and relevant concomitant symptoms

Criteria according to Chapter 5 Section 6 of the Rules of Procedure of the G-BA and Section 6 paragraph 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV):

The appropriate comparator therapy must be an appropriate therapy in the therapeutic indication according to the generally recognised state of medical knowledge (Section 12 SGB V), preferably a therapy for which endpoint studies are available and which has proven its worth in practical application unless contradicted by the guidelines under Section 92, paragraph 1 SGB V or the principle of economic efficiency.

In determining the appropriate comparator therapy, the following criteria, in particular, must be taken into account as specified in Chapter 5 Section 6, paragraph 3 VerfO:

1. To be considered as a comparator therapy, the medicinal product must, principally, have a marketing authorisation for the therapeutic indication.
2. If a non-medicinal treatment is considered as a comparator therapy, this must be available within the framework of the SHI system.
3. As comparator therapy, medicinal products or non-medicinal treatments for which the patient-relevant benefit has already been determined by the G-BA shall be preferred.
4. According to the generally recognised state of medical knowledge, the comparator therapy should be part of the appropriate therapy in the therapeutic indication.

According to Section 6, paragraph 2, sentence 2 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the determination of the appropriate comparator therapy must be based on the actual medical treatment situation as it would be without the medicinal product to be assessed. According to Section 6, paragraph 2, sentence 3 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), the G-BA may exceptionally determine the off-label use of medicinal products as an appropriate comparator therapy or as part of the appropriate comparator therapy if they determine by resolution on the benefit assessment according to Section 7, paragraph 4 that, according to the generally recognised state of medical knowledge, this is considered a therapy standard in the therapeutic indication to be assessed or as part of the therapy standard in the medical treatment situation to be taken into account according to sentence 2, and

1. for the first time, a medicinal product approved in the therapeutic indication is available with the medicinal product to be assessed,
2. according to the generally recognised state of medical knowledge, the off-label use is generally preferable to the medicinal products previously approved for the therapeutic indication, or

3. according to the generally recognised state of medical knowledge, the off-label use for relevant patient groups or indication areas is generally preferable to the medicinal products previously approved for the therapeutic indication.

An appropriate comparator therapy may also be non-medicinal therapy, the best possible add-on therapy including symptomatic or palliative treatment, or monitoring wait-and-see approach.

Justification based on the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO and Section 6, paragraph 2 AM-NutzenV:

On 1. In addition to colchicine, the following product classes or active ingredients are approved for the secondary prevention of atherothrombotic or ischaemic events following a myocardial infarction: Direct factor Xa inhibitors (rivaroxaban), antiplatelet agents (acetylsalicylic acid (ASA), clopidogrel, clopidogrel/ ASA, prasugrel, ticagrelor), vitamin K antagonists (phenprocoumon, warfarin sodium) and heparins (heparin).

Furthermore, for the prevention of ischaemic cardiovascular events following a recent myocardial infarction, active ingredients used to treat the underlying coronary heart disease as well as underlying diseases and comorbidities (e.g. hypertension, heart failure, diabetes mellitus, dyslipoproteinaemias) may be considered, taking into account the suitability of the medicinal product for patients in this therapeutic indication.

On 2. In the context of statutory health insurance, a non-medicinal treatment within the patient group defined by the therapeutic indication is not considered the appropriate comparator therapy.

On 3. The following resolutions/ guidelines of the G-BA are available:

Pharmaceuticals Directive/ Annex I (OTC overview)

2) **Acetylsalicylic acid** (up to 300 mg/ dose unit) as an antiplatelet agent in coronary heart disease (confirmed by clinical symptomatology and supplementary non-invasive or invasive diagnostic tests) and in the after-care following a myocardial infarction and stroke, as well as after arterial procedures.

Pharmaceuticals Directive/ Annex III (prescription restrictions and exclusions in the supply of medicinal products)

21. **Clopidogrel as monotherapy** for the prevention of atherothrombotic events in patients who have had a myocardial infarction, an ischaemic stroke or have confirmed peripheral arterial disease.

This does not apply to patients with

- amputation due to peripheral arterial disease (PAD) or a vascular intervention, or diagnostic confirmation of typical intermittent claudication with pain subsiding within < 10 minutes at rest, or
- intolerance to acetylsalicylic acid, if cost-effective alternatives cannot be used

21a. **Clopidogrel in combination with acetylsalicylic acid** in acute coronary syndrome for the prevention of atherothrombotic events

- except in patients with acute coronary syndrome without ST segment elevation during a treatment period of up to 12 months,

- except in patients with myocardial infarction with ST segment elevation who are eligible for thrombolysis, during a treatment period of up to 28 days.

Pharmaceuticals Directive/ Annex IV (therapeutic information)

- Therapeutic information on prasugrel dated 17 June 2010

Pharmaceuticals Directive/ Annex XII (resolutions on the benefit assessment pursuant to Section 35a SGB V)

- **Ticagrelor**, from 15 December 2011 (prevention of atherothrombotic events in adult patients with acute coronary syndrome)
- **Ticagrelor**, from 15 September 2016 (new therapeutic indication: prevention of atherothrombotic events in adult patients with a history of myocardial infarction (MI) and a high risk of developing an atherothrombotic event)

Directive on Inpatient Treatment Methods:

- The use of antibody-coated and drug-eluting stents for the treatment of coronary artery stenosis
- The use of only antibody-coated stents for the treatment of coronary artery stenosis in patients for whom drug-eluting stents are not an option

On 4. The generally recognised state of medical knowledge was illustrated by a systematic search for guidelines as well as systematic reviews of clinical studies in the present indication and is presented in the "Research and synopsis of the evidence to determine the appropriate comparator therapy according to Section 35a SGB V".

The scientific-medical societies and the Drugs Commission of the German Medical Association (AkdÄ) were also involved in writing on questions relating to the comparator therapy in the present indication according to Section 35a paragraph 7 SGB V (see “Information on Appropriate Comparator Therapy”). Written statements by the German Society for General Practice and Family Medicine (DEGAM) and the Drugs Commission of the German Medical Association (AkdÄ), as well as a joint written statement by the German Cardiac Society (DGK), the German Society for Internal Medicine (DGIM), the German Society for Thoracic, Cardiac and Vascular Surgery (DGTHG) and the German Society for the Prevention and Rehabilitation of Cardiovascular Diseases (DGPR) are available.

As the therapeutic indication specifically addresses secondary prevention following an MI, it is assumed that the acute treatment of acute MI by means of coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI) is not covered by the therapeutic indication.

It should also be noted that colchicine is used as an add-on to standard therapy for the secondary prevention of ischaemic cardiovascular events in adults with atherosclerotic coronary heart disease and a recent MI.

Both the guidelines and clinical experts from the scientific-medical societies and the AkdÄ recommend initiating secondary prevention immediately following acute treatment for an MI. This involves lifestyle changes and medicinal therapy for the underlying diseases and comorbidities, with a view to reducing the risk of further cardiovascular events.

According to the guidelines, medicinal therapy for secondary prevention following an MI comprises dual antiplatelet therapy (DAPT) with ASA and ticagrelor, ASA and prasugrel, or ASA and clopidogrel. The guidelines, the scientific-medical societies and the AkdÄ appear to assign a secondary role to the active ingredient clopidogrel (e.g., recommended only in the case of high bleeding risk or only when an oral anticoagulant is co-administered). The guidelines, the scientific-medical societies and the AkdÄ recommend DAPT for a duration of 12 months; however, if the doctor assesses that there is an increased risk of bleeding, the duration may be reduced to between 1 and 3 months. The DAPT is followed by simple antiplatelet therapy (SAPT) with ASA. The administration of SAPT is only indicated on a case-by-case basis and is only considered as long-term secondary prevention following an MI once DAPT has been completed.

Furthermore, secondary prevention following an MI usually involves a one-year therapy with a beta-blocker, lipid-lowering therapy (usually with a statin), as well as optimal management of all cardiovascular risk factors and appropriate treatment of any existing comorbidities (including hypertension, heart failure and diabetes mellitus).

On the basis of the evidence, the appropriate comparator therapy for colchicine as an add-on therapy in this therapeutic indication is determined to be an optimised standard therapy for the secondary prevention of ischaemic cardiovascular events in atherosclerotic coronary heart disease and a recent MI, as well as for the treatment of any existing comorbidities, e.g., hypertension, heart failure, diabetes mellitus, and relevant concomitant symptoms.

The marketing authorisations and product information must be taken into account.

The findings in Annex XII do not restrict the scope of treatment required to fulfil the medical treatment mandate.

Any change to the appropriate comparator therapy requires a decision by the G-BA based on a prior review of the criteria set out in Chapter 5 Section 6, paragraph 3 VerfO.

2.1.3 Extent and probability of the additional benefit

In summary, the additional benefit of colchicine is assessed as follows:

<u>Adults with atherosclerotic coronary heart disease and a recent myocardial infarction (MI) who are indicated for the prevention of ischaemic cardiovascular events</u>

Hint of a minor additional benefit.

Justification:

For the benefit assessment of colchicine, the pharmaceutical company presented the COLCOT study.

<u>COLCOT study</u>

The multicentre, double-blind, randomised controlled trial COLCOT investigated the efficacy and safety of colchicine compared with placebo in adults with a documented acute MI that had occurred less than 30 days previously. All planned percutaneous revascularisation procedures associated with the MI had to have been completed prior to enrolment in the study. Excluded were, among others, subjects with a type 2 index MI (secondary due to ischaemic imbalance), haemodynamic instability, cardiogenic shock, NYHA class III–IV heart

failure, a stroke within the last 3 months, or planned coronary artery bypass surgery or such surgery performed less than 3 years previously.

Following a 2-week screening phase, the subjects were randomised in a 1:1 ratio to receive treatment with colchicine (N = 2,366) or a placebo (N = 2,379). In addition, patients in both study arms received a standard therapy for the secondary prevention of ischaemic cardiovascular events (antiplatelet therapy, statins, RAAS inhibitors (preferably ACE inhibitors) and beta-blockers) in accordance with national guidelines and, where necessary, standard treatment for any existing comorbidities, e.g., dyslipidaemia, hypertension, angina pectoris and diabetes mellitus, at the doctor's discretion. Concomitant treatment should be kept as stable as possible throughout the study.

The event-driven study was conducted at 167 study sites in the United States, South America, Europe and the United Kingdom, among other locations, between December 2015 and July 2019. For the benefit assessment, the pharmaceutical company submitted the analyses as of the final data cut-off (28 August 2019) at which the planned number of 301 events for the primary endpoint had been reached.

Patients in both study arms of the COLCOT study received a standard therapy for the secondary prevention of ischaemic cardiovascular events in atherosclerotic coronary heart disease and a recent MI, as well as for the treatment of any existing comorbidities, e.g., dyslipidaemia, hypertension, heart failure and relevant concomitant symptoms. Despite the lack of data on laboratory parameters such as LDL-C levels and blood pressure for the assessment of concomitant treatments, there is no overall indication that the concomitant treatment was inadequate in a significant percentage of patients. Moreover, it is assumed that the concomitant treatment used in the study is in line with the guideline recommendations.

In the COLCOT study, the percentage of patients with type 2 diabetes mellitus was approximately 19% in the intervention arm and approximately 20% in the control arm. The guidelines recommend the administration of SGLT-2 inhibitors or GLP-1 receptor agonists for patients with type 2 diabetes mellitus and cardiovascular disease. However, these were administered only to a small number of patients with type 2 diabetes mellitus in the COLCOT study. It is assumed that the concomitant treatments used in the study largely reflect guideline recommendations. This is supported by the fact that, contrary to guideline recommendations, patients with type 2 diabetes mellitus, who were not treated with an SGLT-2 inhibitor or a GLP-1 receptor agonist, represent only a relatively small percentage of the total study population.

Extent and probability of the additional benefit

Mortality

For the overall mortality, there were no statistically significant differences between the treatment arms of the COLCOT study.

Morbidity

Major adverse cardiovascular events

The dossier contains analyses of the primary and secondary composite endpoints of the COLCOT study, as well as their sub-components. These composite endpoints consist of the following individual endpoints: "cardiovascular death", "resuscitated cardiac arrest", "acute myocardial infarction", "stroke" and, additionally in the primary endpoint, "urgent hospital admission for angina pectoris requiring coronary revascularisation". With the exception of the endpoint "cardiovascular death", the events are to be classified as "non-fatal".

The endpoint "urgent hospital admission for angina pectoris requiring coronary revascularisation" represents a clinically relevant and therefore important subset of all patients with angina pectoris. For this endpoint, there are uncertainties overall regarding the potentially incomplete collection of all events of unstable angina pectoris that led to hospitalisation. Notwithstanding this, the endpoint is used for the benefit assessment.

For the endpoints "stroke (non-fatal)" and "urgent hospital admission for angina pectoris requiring coronary revascularisation", there was a statistically significant advantage in favour of colchicine in each case.

The results for the endpoints "cardiovascular death", "resuscitated cardiac arrest" and "acute myocardial infarction" show no statistically significant differences between the treatment groups, but indicate the same direction of effect as the other individual components.

For the composite primary endpoint "major adverse cardiovascular events", there was a statistically significant advantage in favour of colchicine.

Recurrent cardiovascular events

The dossier also contains analyses of recurrent cardiovascular events, defined as the occurrence of multiple events for the primary composite endpoint in a patient. All events were considered, including those that occurred after the first event.

As the results are therefore based on the occurrence of multiple events for the primary composite endpoint in a single patient, the endpoint is only presented additionally.

Severe heart failure events

The pharmaceutical company presented data on the endpoint "hospital admission for heart failure" in the dossier. However, the operationalisation presented also includes urgent, unscheduled visits to the outpatient clinic/ doctor's surgery or the accident and emergency department. There is no information available on how many patients were actually hospitalised following a visit to their doctor or the accident and emergency department. There are therefore no suitable data available on the incidence of severe heart failure events, operationalised as hospitalisation for heart failure.

Coronary revascularisation

For the endpoint of coronary revascularisation, operationalised as coronary artery bypass grafting or PCI, the study included both urgent and elective coronary revascularisation procedures. In the study, these events, which may subsequently require coronary revascularisation, were also collected under the endpoint "myocardial infarction" and were already taken into account in the benefit assessment. Consequently, the endpoint "coronary revascularisation" is not considered separately for the benefit assessment.

Deep vein thrombosis or pulmonary embolism

The dossier contains analyses of the composite endpoint, comprising the individual components "deep vein thrombosis" and "pulmonary embolism". However, the pharmaceutical company did not provide any analyses of the individual components or of the patients who experienced a qualifying event.

<u>Quality of life</u>

The endpoint of health-related quality of life was not assessed in the COLCOT study.

Side effects

Adverse events (AEs) regardless of severity

In the COLCOT study, AEs were not systematically collected, regardless of their severity. Only AEs that affected the gastrointestinal system and were either assessed by the principal investigator as related to the study medication or classified as clinically significant laboratory value nonconformities were collected. However, this approach is inappropriate, as it means that frequent, patient-relevant, non-serious AEs cannot be systematically identified in the study. No data are therefore available for the overall rates of AEs and severe AEs as they were not collected.

Serious adverse events (SAEs)

During the collection of SAEs, a significant number of disease-related events within the SOC[2] "cardiac disorders" were also captured in the study, and these data were presented in the dossier. However, analyses that clearly do not take into account disease-related events are required for the benefit assessment. As part of the written statement procedure, the pharmaceutical company submitted new analyses of SAEs, excluding disease-related events. Disease-related events were defined in this context as those SOCs and PTs[2] that are potentially associated with a non-fatal MI. For the endpoint of SAEs (excluding disease-related events), the results showed no statistically significant differences between the treatment groups.

Discontinuation due to AEs

The analyses in the dossier relating to the endpoint "discontinuation due to AEs" may be incomplete. On the one hand, this is due to the selective collection of AEs - regardless of their severity - in the COLCOT study and, on the other, to the fact that data on the final discontinuation of the study medication were only collected from visit 5 onwards (6 months after randomisation). Furthermore, AEs that led to therapy discontinuation were not collected in detail by SOC and PT.

Although the pharmaceutical company submitted analyses of the overall rate excluding disease-related events and of the percentages of events broken down by SOC and PT in the written statement procedure, the data submitted subsequently do not address the uncertainty arising from the potentially incomplete assessment of endpoints in the study. Overall, there continue to be no suitable data available for the endpoint of discontinuation due to AEs.

Gastrointestinal disorders (SOC, AE)

For the SOC of gastrointestinal disorders, there were no statistically significant differences between the treatment groups.

Overall assessment

For the benefit assessment, the pharmaceutical company presented the double-blind, randomised controlled trial COLCOT, which compared colchicine with placebo in adults with a documented acute MI that occurred less than 30 days previously. All study participants also received a standard therapy for the secondary prevention of ischaemic cardiovascular events and, where necessary, standard treatment for any existing comorbidities.

[2] SOC (system organ class) and PT (preferred term) according to MedDRA

For the overall mortality, there was no statistically significant difference between the treatment groups of the COLCOT study.

For the primary composite endpoint "major adverse cardiovascular events", including the individual components "stroke (non-fatal)" and "urgent hospital admission for angina pectoris requiring coronary revascularisation" in the endpoint category of morbidity, there was a statistically significant advantage in favour of colchicine. For the individual components "cardiovascular death", "resuscitated cardiac arrest" and "acute myocardial infarction" of the primary composite endpoint, there were no statistically significant differences between the treatment groups. For the endpoint "severe heart failure events", no suitable data were available for the benefit assessment.

The endpoint of health-related quality of life was not assessed in the COLCOT study.

For the endpoint category of side effects, there was no systematic collection of the AEs in the COLCOT study, regardless of their severity. For the overall rates of severe AEs and for the endpoint of discontinuation due to AEs, there were therefore no data available for the benefit assessment. For the overall rates of serious AEs, there was no statistically significant difference between the treatment groups.

For the primary composite endpoint "major adverse cardiovascular events", including the individual components "stroke (non-fatal)" and "urgent hospital admission for angina pectoris requiring coronary revascularisation", data from the COLCOT study showed an advantage in favour of colchicine overall. The extent of the benefit is considered to be minor due to the absolute risk reduction.

In the overall assessment, the G-BA therefore identified a minor additional benefit of colchicine as an add-on to optimised standard therapy, compared with the appropriate comparator therapy, in adults with atherosclerotic coronary heart disease and a recent myocardial infarction (MI) who are indicated for prevention of ischaemic cardiovascular events.

Reliability of data (probability of the additional benefit)

For the COLCOT study and for all endpoints for which suitable data are available, the risk of bias is assessed as low.

Although it is assumed that the concomitant treatments used in the COLCOT study largely reflect the guideline recommendations, there are uncertainties regarding the reliability of data from the study. On the one hand, there is a lack of data on laboratory parameters such as LDL-C levels and blood pressure required for the assessment of concomitant treatments, as well as data on therapy adjustment (initiating and switching therapy, and dose adjustments) over the course of the study. On the other, uncertainties arise due to the lack of systematic data collection and the unclear time periods for collecting the data on side effects. Furthermore, with regard to the endpoint "urgent hospital admission for angina pectoris requiring coronary revascularisation", there are uncertainties regarding potentially incomplete collection of all events of unstable angina pectoris that led to hospitalisation.

Based on these uncertainties, the significance of the evidence is classified in the "hint" category overall.

2.1.4 Summary of the assessment

The present assessment concerns the benefit assessment of the known active ingredient colchicine (Colxi). Colchicine is approved for the prevention of ischaemic cardiovascular events in adults with atherosclerotic coronary heart disease and a recent myocardial infarction (MI), in addition to standard therapies.

The G-BA determined the appropriate comparator therapy to be an optimised standard therapy for the secondary prevention of ischaemic cardiovascular events in patients with atherosclerotic coronary heart disease and a recent myocardial infarction (MI), as well as for the treatment of any existing comorbidities, e.g., hypertension, heart failure, diabetes mellitus and relevant concomitant symptoms.

For the benefit assessment, the pharmaceutical company presented the double-blind, randomised controlled trial COLCOT, which compared colchicine with placebo in adults with a documented acute MI that occurred less than 30 days previously. All study participants also received a standard therapy for the secondary prevention of ischaemic cardiovascular events and, where necessary, standard treatment for any existing comorbidities.

For the overall mortality, there was no statistically significant difference between the treatment groups of the COLCOT study.

For the primary composite endpoint "major adverse cardiovascular events", including the individual components "stroke (non-fatal)" and "urgent hospital admission for angina pectoris requiring coronary revascularisation" in the endpoint category of morbidity, there was a statistically significant advantage in favour of colchicine. The extent of the benefit is considered to be minor due to the absolute risk reduction. For the results of the other morbidity endpoints, either no statistically significant differences between the treatment groups were observed, or no suitable data were available.

The endpoint of health-related quality of life was not assessed in the COLCOT study.

For the endpoint category of side effects, there was no systematic collection of the AEs in the COLCOT study, regardless of their severity. For the overall rates of severe AEs and for the endpoint of discontinuation due to AEs, there were therefore no data available for the benefit assessment. For the overall rates of serious AEs, there was no statistically significant difference between the treatment groups.

Due to existing uncertainties, the reliability of the results of the COLCOT study is classified as a hint. On the one hand, uncertainties arise due to a lack of data on laboratory parameters for assessing concomitant treatments, as well as data on therapy adjustment over the course of the study. On the other, uncertainties arise due to the lack of systematic data collection and the unclear time periods for collecting the data on side effects. Furthermore, with regard to the endpoint "urgent hospital admission for angina pectoris requiring coronary revascularisation", there are uncertainties regarding potentially incomplete collection of all events of unstable angina pectoris that led to hospitalisation.

Taken together, the demonstrated advantage in the endpoint category of morbidity in the COLCOT study gives a hint of a minor additional benefit of colchicine as an add-on to optimised standard therapy, compared with the appropriate comparator therapy.

2.2 Number of patients or demarcation of patient groups eligible for treatment

The number of patients is the target population in statutory health insurance (SHI).

The patient numbers presented in the dossier are considered to be unreliable. In particular, there are uncertainties arising from the 7-day mortality rates used as a basis and the inconsistent criteria for identifying patients with myocardial infarction in non-obstructive coronary arteries (MINOCA). Due to the additional uncertainties regarding the inclusion of patients with contraindications, the resolution is based on the patient numbers derived from the dossier within the therapeutic indication according to Section 4.1 of the product information, without taking the contraindications into account.

Overall, the stated range of 125,000 to 132,000 patients is fraught with uncertainty.

2.3 Requirements for a quality-assured application

The requirements in the product information are to be taken into account.

Colchicine has a narrow therapeutic index and is therefore associated with a significant risk of severe overdose. The recommended maximum dose must not be exceeded. Therefore, a review of any concomitant medication and an assessment of kidney and liver function should be carried out before initiation of therapy.

2.4 Treatment costs

The treatment costs are based on the contents of the product information and the information listed in the LAUER-TAXE® (last revised: 15 June 2026).

According to the product information, the recommended dose of colchicine is 0.5 mg, administered once daily as a tablet.

The appropriate comparator therapy of "an optimised standard therapy for the secondary prevention of ischaemic cardiovascular events in patients with atherosclerotic coronary heart disease and a recent myocardial infarction (MI), as well as for the treatment of any existing concomitant diseases, e.g., hypertension, heart failure, diabetes mellitus and relevant concomitant symptoms" encompasses a wide range of inherently different treatment options. Secondary prevention following an MI is usually achieved through DAPT with ASA and ticagrelor, ASA and prasugrel or ASA and clopidogrel for 12 months; however, if the doctor assesses that there is an increased risk of bleeding, the duration of treatment may be reduced to between 1 and 3 months. The DAPT is followed by a SAPT with ASA. Furthermore, secondary prevention following an MI usually involves a one-year therapy with a beta-blocker, lipid-lowering therapy, as well as optimal management of all cardiovascular risk factors and appropriate treatment of any existing comorbidities (including hypertension, heart failure and diabetes mellitus).

It is not possible in this instance to state any specific costs for the appropriate comparator therapy due to the patient-individually optimised standard therapy for the secondary prevention of ischaemic cardiovascular events in patients with atherosclerotic coronary heart disease and a recent MI, and of any existing comorbidities. In addition, the optimised standard therapy is provided both within the scope of the assessed medicinal product colchicine and as part of the appropriate comparator therapy.

Treatment period:

Adults with atherosclerotic coronary heart disease and a recent myocardial infarction (MI) who are indicated for the prevention of ischaemic cardiovascular events

Designation of the therapy	Treatment mode	Number of treatments/ patient/ year	Treatment duration/ treatment (days)	Treatment days/ patient/ year
Medicinal product to be assessed				
Colchicine	Continuously, 1 x daily	365.0	1	365.0
+ optimised standard therapy	Different from patient to patient			
Appropriate comparator therapy				
Optimised standard therapy	Different from patient to patient			

Consumption:

Adults with atherosclerotic coronary heart disease and a recent myocardial infarction (MI) who are indicated for the prevention of ischaemic cardiovascular events

Designation of the therapy	Dosage/ application	Dose/ patient/ treatment days	Consumption by potency/ treatment day	Treatment days/ patient/ year	Average annual consumption by potency
Medicinal product to be assessed					
Colchicine	0.5 mg	0.5 mg	1 x 0.5 mg	365.0	365 x 0.5 mg
+ optimised standard therapy	Different from patient to patient				
Appropriate comparator therapy					
Optimised standard therapy	Different from patient to patient				

Costs:

In order to improve comparability, the costs of the medicinal products were approximated both on the basis of the pharmacy sales price level and also deducting the statutory rebates in accordance with Section 130 and Section 130a SGB V. To calculate the annual treatment costs, the required number of packs of a particular potency was first determined on the basis of consumption. Having determined the number of packs of a particular potency, the costs of the medicinal products were then calculated on the basis of the costs per pack after deduction of the statutory rebates. Any reference prices shown in the cost representation may not represent the cheapest available alternative.

Costs of the medicinal products:

Adults with atherosclerotic coronary heart disease and a recent myocardial infarction (MI) who are indicated for the prevention of ischaemic cardiovascular events

Designation of the therapy	Packaging size	Costs (pharmacy sales price)	Rebate Section 130 SGB V	Rebate Section 130a SGB V	Costs after deduction of statutory rebates
Medicinal product to be assessed					
Colchicine	100 FCT	€ 388.08	€ 1.77	€ 20.86	€ 365.45
+ optimised standard therapy	Different from patient to patient				
Appropriate comparator therapy					
Optimised standard therapy	Different from patient to patient				
Abbreviations: FCT = film-coated tablets					

LAUER-TAXE® last revised: 15 June 2026

Costs for additionally required SHI services:

Only costs directly related to the use of the medicinal product are taken into account. If there are regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, the costs incurred for this must be taken into account as costs for additionally required SHI services.

Medical treatment costs, medical fee services, and costs incurred for routine examinations (e.g. regular laboratory services such as blood count tests) that do not exceed the standard expenditure in the course of the treatment are not shown.

Because there are no regular differences in the necessary use of medical treatment or in the prescription of other services in the use of the medicinal product to be evaluated and the appropriate comparator therapy in accordance with the product information, no costs for additionally required SHI services had to be taken into account.

3. Bureaucratic costs calculation

The proposed resolution does not create any new or amended information obligations for care providers within the meaning of Annex II to Chapter 1 VerfO and, accordingly, no bureaucratic costs.

4. Process sequence

At their session on 12 August 2025, the Subcommittee on Medicinal Products determined the appropriate comparator therapy.

On 27 February 2026, the pharmaceutical company submitted a dossier for the benefit assessment of colchicine to the G-BA in due time in accordance with Chapter 5, Section 8, paragraph 1, number 7 VerfO.

By letter dated 27 February 2026 in conjunction with the resolution of the G-BA of 1 August 2011 concerning the commissioning of the IQWiG to assess the benefit of medicinal products with new active ingredients in accordance with Section 35a SGB V, the G-BA commissioned the IQWiG to assess the dossier concerning the active ingredient colchicine.

The dossier assessment by the IQWiG was submitted to the G-BA on 28 May 2026, and the written statement procedure was initiated with publication on the G-BA website on 1 June 2026. The deadline for submitting written statements was 22 June 2026.

The oral hearing was held on 6 July 2026.

By letter dated 7 July 2026, the IQWiG was commissioned with a supplementary assessment of data submitted in the written statement procedure. The addendum prepared by the IQWiG was submitted to the G-BA on 31 July 2026.

In order to prepare a recommendation for a resolution, the Subcommittee on Medicinal Products commissioned a working group (Section 35a) consisting of the members nominated by the leading organisations of the care providers, the members nominated by the SHI umbrella organisation, and representatives of the patient organisations. Representatives of the IQWiG also participate in the sessions.

The evaluation of the written statements received and the oral hearing were discussed at the Subcommittee's session on 11 August 2026, and deliberation of the draft resolution was concluded.

At their session on 20 August 2026, the plenum adopted a resolution to amend the Pharmaceuticals Directive.

Chronological course of consultation

Session	Date	Subject of consultation
Subcommittee on Medicinal Products	12 August 2025	Determination of the appropriate comparator therapy
Working group Section 35a	1 July 2026	Information on written statements received; preparation of the oral hearing
Subcommittee on Medicinal Products	6 July 2026 7 July 2026	Conduct of the oral hearing, commissioning of the IQWiG with the supplementary assessment of documents
Working group Section 35a	15 July 2026 5 August 2026	Consultation on the dossier assessment by the IQWiG and evaluation of the written statement procedure
Subcommittee on Medicinal Products	11 August 2026	Concluding discussion of the draft resolution
Plenum	20 August 2026	Adoption of the resolution on the amendment of the Pharmaceuticals Directive

Berlin, 20 August 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Dr Optendrenk