IQWiG Reports – Commission No. A19-53

Dapagliflozin (type 2 diabetes mellitus) –

Benefit assessment according to §35a Social Code Book V[1] (new scientific findings)

Extract

[1] Translation of Sections 2.1 to 2.8 of the dossier assessment *Dapagliflozin (Diabetes mellitus Typ 2) – Nutzenbewertung gemäß § 35a SGB V (neue wissenschaftliche Erkenntnisse)* (Version 1.0; Status: 27 September 2019). Please note: This translation is provided as a service by IQWiG to English-language readers. However, solely the German original text is absolutely authoritative and legally binding.

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Table of contents

Page

List of tables[2]

Page

[2] Table numbers start with “2” as numbering follows that of the full dossier assessment.

List of abbreviations

Abbreviation	Meaning
ACT	appropriate comparator therapy
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
ICTRP	International Clinical Trials Registry Platform
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
RCT	randomized controlled trial
SGB	Sozialgesetzbuch (Social Code Book)

2 Benefit assessment

2.1 Executive summary of the benefit assessment

Background

In accordance with §35a Social Code Book (SGB) V, the Federal Joint Committee (G-BA) commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug dapagliflozin. Two benefit assessments of dapagliflozin in the therapeutic indication of type 2 diabetes mellitus have already been conducted (G-BA decisions from 6 June 2013 and 21 June 2018). Due to new scientific findings, the pharmaceutical company (hereinafter referred to as "the company") now requested a new assessment for the entire approved therapeutic indication. The assessment was based on a dossier compiled by the company. The dossier was sent to IQWiG on 18 June 2019.

Research question

The aim of the present report is the assessment of the added benefit of dapagliflozin in comparison with the appropriate comparator therapy (ACT) for the treatment of adults with type 2 diabetes mellitus in the following approved subindications:

- **monotherapy:** when diet and exercise alone are insufficient in patients for whom use of metformin is considered inappropriate due to intolerance
- **add-on combination therapy:** in combination with other blood-glucose lowering medicinal products, when these, together with diet and exercise, do not provide adequate glycaemic control

The G-BA distinguished between different patient groups in its specification of the ACTs. This resulted in 5 research questions, which are presented in Table 2.

Table 2: Research questions of the benefit assessment of dapagliflozin

Research question	**Subindication**[a]	**ACT**[b]
1	Monotherapy when diet and exercise alone do not provide adequate glycaemic control and the use of metformin is considered inappropriate due to intolerance	▪ Sulfonylurea (glibenclamide or glimepiride)
2	Combination with one other blood-glucose lowering drug (except insulin, here metformin), when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Metformin + sulfonylurea (glibenclamide or glimepiride) or ▪ metformin + empagliflozin or ▪ metformin + liraglutide[c]
3	Combination with one other blood-glucose lowering drug (except insulin and metformin), when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Metformin + sulfonylurea (glibenclamide or glimepiride) or ▪ metformin + empagliflozin or ▪ metformin + liraglutide[c] or ▪ human insulin if metformin is not tolerated or contraindicated according to the SPC
4	Combination with at least 2 other blood-glucose lowering drugs (except insulin), when these, together with diet and exercise, do not provide adequate glycaemic control	▪ Human insulin + metformin or ▪ human insulin + empagliflozin[c] or ▪ human insulin + liraglutide[c] or ▪ human insulin if, according to the SPC, the specified combination partners are not tolerated, contraindicated or not sufficiently effective due to advanced type 2 diabetes mellitus
5	Combination with insulin, without or with one other blood-glucose lowering drug, when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Optimization of the human insulin regimen (if applicable + metformin or empagliflozin[c] or liraglutide[c])

a: Subdivisions of the therapeutic indication according to the G-BA.
b: Presentation of the respective ACT specified by the G-BA.
c: Empagliflozin or liraglutide, each in combination with other medication for the treatment of cardiovascular risk factors, in particular antihypertensive medications, anticoagulants and/or lipid-lowering drugs, and only for patients with manifest cardiovascular disease (for the operationalization, see inclusion criteria of the relevant studies for empagliflozin [1] and liraglutide [2]).
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; SPC: Summary of Product Characteristics

On the one hand, the company did not follow the G-BA's specification on the division of the therapeutic indication into different patient groups and on the ACTs. On the other, the company, in contrast to its request for a new assessment and to the G-BA's decision, did not address the entire therapeutic indication of type 2 diabetes mellitus, but restricted its statements to patients at increased cardiovascular risk.

In accordance with the G-BA's commission, the present assessment was conducted based on the patient groups and the ACTs specified by the G-BA.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. Randomized controlled trials (RCTs) with a minimum duration of 24 weeks were used for the derivation of the added benefit.

Results

In its dossier, the company did not investigate any of the research questions presented in Table 2 and hence did not present any data for the assessment of the added benefit of dapagliflozin in comparison with the ACT. This resulted in no hint of an added benefit of dapagliflozin in comparison with the ACT for any of the G-BA's research questions; an added benefit is therefore not proven.

Probability and extent of added benefit, patient groups with therapeutically important added benefit[3]

Based on the results presented, probability and extent of the added benefit of the drug dapagliflozin in comparison with the ACT are assessed as follows:

None of the research questions presented above was subject of the company's dossier; so the content of the dossier was incomplete. Since the company did not investigate the research questions and therefore did not present any data for the assessment of the added benefit of dapagliflozin in comparison with the ACT for the treatment of adults with type 2 diabetes mellitus, an added benefit of dapagliflozin is not proven.

Table 3 shows a summary of probability and extent of the added benefit of dapagliflozin.

[3] On the basis of the scientific data analysed, IQWiG draws conclusions on the (added) benefit or harm of an intervention for each patient-relevant outcome. Depending on the number of studies analysed, the certainty of their results, and the direction and statistical significance of treatment effects, conclusions on the probability of (added) benefit or harm are graded into 4 categories: (1) "proof", (2) "indication", (3) "hint", or (4) none of the first 3 categories applies (i.e., no data available or conclusions 1 to 3 cannot be drawn from the available data). The extent of added benefit or harm is graded into 3 categories: (1) major, (2) considerable, (3) minor (in addition, 3 further categories may apply: non-quantifiable extent of added benefit, added benefit not proven, or less benefit). For further details see [3,4].

Table 3: Dapagliflozin – probability and extent of added benefit

Research question	Subindication[a]	ACT[b]	Probability and extent of added benefit
1	Monotherapy when diet and exercise alone do not provide adequate glycaemic control and the use of metformin is considered inappropriate due to intolerance	▪ Sulfonylurea (glibenclamide or glimepiride)	Added benefit not proven
2	Combination with one other blood-glucose lowering drug (except insulin, here metformin), when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Metformin + sulfonylurea (glibenclamide or glimepiride) or ▪ metformin + empagliflozin or ▪ metformin + liraglutide[c]	Added benefit not proven
3	Combination with one other blood-glucose lowering drug (except insulin and metformin), when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Metformin + sulfonylurea (glibenclamide or glimepiride) or ▪ metformin + empagliflozin or ▪ metformin + liraglutide[c] or ▪ human insulin if metformin is not tolerated or contraindicated according to the SPC	Added benefit not proven
4	Combination with at least 2 other blood-glucose lowering drugs (except insulin), when these, together with diet and exercise, do not provide adequate glycaemic control	▪ Human insulin + metformin or ▪ human insulin + empagliflozin[c] or ▪ human insulin + liraglutide[c] or ▪ human insulin if, according to the SPC, the specified combination partners are not tolerated, contraindicated or not sufficiently effective due to advanced type 2 diabetes mellitus	Added benefit not proven
5	Combination with insulin, without or with one other blood-glucose lowering drug, when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Optimization of the human insulin regimen (if applicable + metformin or empagliflozin[c] or liraglutide[c])	Added benefit not proven

a: Subdivisions of the therapeutic indication according to the G-BA.
b: Presentation of the respective ACT specified by the G-BA.
c: Empagliflozin or liraglutide, each in combination with other medication for the treatment of cardiovascular risk factors, in particular antihypertensive medications, anticoagulants and/or lipid-lowering drugs, and only for patients with manifest cardiovascular disease (for the operationalization, see inclusion criteria of the relevant studies for empagliflozin [1] and liraglutide [2]).
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; SPC: Summary of Product Characteristics

The G-BA decides on the added benefit.

Research question of the company

Instead of the G-BA's research questions presented above, the company investigated the following research question in its dossier: dapagliflozin in addition to standard therapy in adult

patients with type 2 diabetes mellitus and increased cardiovascular risk in comparison with treatment with placebo in addition to standard therapy. The company defined standard therapy as individual background therapy for the treatment of type 2 diabetes mellitus and other cardiovascular risk factors and comorbidities in accordance with relevant guidelines. The company presented the DECLARE-TIMI 58 study for this research question.

Adult patients with type 2 diabetes mellitus and increased cardiovascular risk are comprised by the therapeutic indication of dapagliflozin and therefore as a subgroup by all 5 research questions mentioned above. In accordance with the G-BA's specification, the added benefit for this subpopulation also has to be shown in comparison with the respective ACT. The company did not present such analyses. Due to the way it was conducted, the DECLARE-TIMI 58 is unsuitable for this purpose, however.

Irrespective of this, the DECLARE-TIMI 58 study is also unsuitable for the comparison with standard therapy intended by the company. The study defined standard therapy as individual treatment at the investigator's discretion in accordance with local practice and local guidelines with the study protocol defining additional target levels. Both regarding blood-glucose lowering and blood pressure treatment, the results of the DECLARE-TIMI 58 study suggested that implementation of the prerequisites described in the study protocol was insufficient. There were also signs that, contrary to the prerequisites in the study protocol, the substance-specific effects of dapagliflozin were not compensated by an intensified treatment in the comparator group. Besides, with regard to blood-glucose lowering therapy, drugs defined by the G-BA as part of the ACT for patients at increased cardiovascular risk (empagliflozin, liraglutide), were hardly used. Overall, it can therefore not be assumed for both aspects (blood-glucose lowering therapy, concomitant cardiovascular treatment) that the therapy used in the comparator group was an adequate standard therapy.

2.2 Research question

The aim of the present report is the assessment of the added benefit of dapagliflozin in comparison with the ACT for the treatment of adults with type 2 diabetes mellitus in the following approved subindications:

- **monotherapy:** when diet and exercise alone are insufficient in patients for whom use of metformin is considered inappropriate due to intolerance
- **add-on combination therapy:** in combination with other blood-glucose lowering medicinal products, when these, together with diet and exercise, do not provide adequate glycaemic control

The G-BA distinguished between different patient groups in its specification of the ACTs. This resulted in 5 research questions, which are presented in Table 4.

Table 4: Research questions of the benefit assessment of dapagliflozin

Research question	Subindication[a]	ACT[b]
1	Monotherapy when diet and exercise alone do not provide adequate glycaemic control and the use of metformin is considered inappropriate due to intolerance	▪ Sulfonylurea (glibenclamide or glimepiride)
2	Combination with one other blood-glucose lowering drug (except insulin, here metformin), when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Metformin + sulfonylurea (glibenclamide or glimepiride) or ▪ metformin + empagliflozin or ▪ metformin + liraglutide[c]
3	Combination with one other blood-glucose lowering drug (except insulin and metformin), when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Metformin + sulfonylurea (glibenclamide or glimepiride) or ▪ metformin + empagliflozin or ▪ metformin + liraglutide[c] or ▪ human insulin if metformin is not tolerated or contraindicated according to the SPC
4	Combination with at least 2 other blood-glucose lowering drugs (except insulin), when these, together with diet and exercise, do not provide adequate glycaemic control	▪ Human insulin + metformin or ▪ human insulin + empagliflozin[c] or ▪ human insulin + liraglutide[c] or ▪ human insulin if, according to the SPC, the specified combination partners are not tolerated, contraindicated or not sufficiently effective due to advanced type 2 diabetes mellitus
5	Combination with insulin, without or with one other blood-glucose lowering drug, when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Optimization of the human insulin regimen (if applicable + metformin or empagliflozin[c] or liraglutide[c])

a: Subdivisions of the therapeutic indication according to the G-BA.
b: Presentation of the respective ACT specified by the G-BA.
c: Empagliflozin or liraglutide, each in combination with other medication for the treatment of cardiovascular risk factors, in particular antihypertensive medications, anticoagulants and/or lipid-lowering drugs, and only for patients with manifest cardiovascular disease (for the operationalization, see inclusion criteria of the relevant studies for empagliflozin [1] and liraglutide [2]).
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; SPC: Summary of Product Characteristics

On the one hand, the company did not follow the G-BA's specification on the division of the therapeutic indication into different patient groups and on the ACTs. On the other, the company, in contrast to its request for a new assessment and to the G-BA's decision [5], did not address the entire therapeutic indication of type 2 diabetes mellitus, but restricted its statements to patients at increased cardiovascular risk.

In accordance with the G-BA's commission, the present assessment was conducted based on the patient groups and the ACTs specified by the G-BA.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier. RCTs with a minimum duration of 24 weeks were used for the derivation of the added benefit.

Research question of the company

Instead of the G-BA's research questions presented above, the company investigated the following research question in its dossier: dapagliflozin in addition to standard therapy in adult patients with type 2 diabetes mellitus and increased cardiovascular risk in comparison with treatment with placebo in addition to standard therapy. The company defined standard therapy as individual background therapy for the treatment of type 2 diabetes mellitus and other cardiovascular risk factors and comorbidities in accordance with relevant guidelines. The company presented the DECLARE-TIMI 58 study for this research question.

Adult patients with type 2 diabetes mellitus and increased cardiovascular risk are comprised by the therapeutic indication of dapagliflozin and therefore as a subgroup by all 5 research questions mentioned above. In accordance with the G-BA's specification, the added benefit for this subpopulation also has to be shown in comparison with the respective ACT. The company did not present such analyses. Due to the way it was conducted, the DECLARE-TIMI 58 is unsuitable for this purpose, however. Irrespective of this, the DECLARE-TIMI 58 study is also unsuitable for the comparison with standard therapy intended by the company (see Appendix A of the full dossier assessment).

Irrespective of this, due to the size and the outcomes investigated (particularly cardiovascular events and all-cause mortality), the DECLARE-TIMI 58 study is described in Appendix A of the full dossier assessment.

2.3 Research question 1: dapagliflozin monotherapy

2.3.1 Information retrieval and study pool (research question 1)

The company did not investigate the present research question in its benefit assessment.

To check whether there are RCTs of direct comparison for research question 1, a search on dapagliflozin was conducted in the trial registries ClinicalTrials.gov, International Clinical Trials Registry Platform (ICTRP) Search Portal, EU Clinical Trials Register, and PharmNet.Bund – Klinische Prüfungen (last search on 16 July 2019).

No relevant study was identified from the check.

2.3.2 Results on added benefit (research question 1)

The company did not investigate the research question in its benefit assessment, and hence did not present any data for the assessment of the added benefit of dapagliflozin in comparison with the ACT. This resulted in no hint of an added benefit of dapagliflozin monotherapy for adults

with type 2 diabetes mellitus in comparison with the ACT; an added benefit is therefore not proven.

2.3.3 Probability and extent of added benefit (research question 1)

The present research question was not subject of the company's benefit assessment; so the content of the dossier was incomplete. Irrespective of this, the Institute's search identified no RCT of direct comparison on research question 1. Overall, an added benefit of dapagliflozin monotherapy for adults with type 2 diabetes mellitus in comparison with the ACT is not proven.

2.3.4 List of included studies (research question 1)

Not applicable as the company presented no relevant data for the benefit assessment.

2.4 Research question 2: dapagliflozin plus metformin

2.4.1 Information retrieval and study pool (research question 2)

The company did not investigate the present research question in its benefit assessment.

To check whether there are RCTs of direct comparison for research question 2, a search on dapagliflozin was conducted in the trial registries ClinicalTrials.gov, ICTRP Search Portal, EU Clinical Trials Register, and PharmNet.Bund – Klinische Prüfungen (last search on 16 July 2019).

No suitable study was identified from the check.

The D1689C00014 (DapaZu) study was identified in the search for relevant studies. The study was already the subject of a previous benefit assessment of dapagliflozin; information on the unsuitability of this study can be found in dossier assessment A17-65 [6].

2.4.2 Results on added benefit (research question 2)

The company did not investigate the research question in its benefit assessment, and hence did not present any data for the assessment of the added benefit of dapagliflozin in comparison with the ACT. This resulted in no hint of an added benefit of dapagliflozin plus metformin for adults with type 2 diabetes mellitus in comparison with the ACT; an added benefit is therefore not proven.

2.4.3 Probability and extent of added benefit (research question 2)

The present research question was not subject of the company's benefit assessment; so the content of the dossier was incomplete. Irrespective of this, the Institute's search identified no RCT of direct comparison on research question 2. Overall, an added benefit of dapagliflozin plus metformin for adults with type 2 diabetes mellitus in comparison with the ACT is not proven.

2.4.4 List of included studies (research question 2)

Not applicable as the company presented no relevant data for the benefit assessment.

2.5 Research question 3: dapagliflozin plus one other blood-glucose lowering drug except insulin and metformin

2.5.1 Information retrieval and study pool (research question 3)

The company did not investigate the present research question in its benefit assessment.

To check whether there are RCTs of direct comparison for research question 3, a search on dapagliflozin was conducted in the trial registries ClinicalTrials.gov, ICTRP Search Portal, EU Clinical Trials Register, and PharmNet.Bund – Klinische Prüfungen (last search on 16 July 2019).

No relevant study was identified from the check.

2.5.2 Results on added benefit (research question 3)

The company did not investigate the research question in its benefit assessment, and hence did not present any data for the assessment of the added benefit of dapagliflozin in comparison with the ACT. This resulted in no hint of an added benefit of dapagliflozin plus one other blood-glucose lowering drug except insulin and metformin for adults with type 2 diabetes mellitus in comparison with the ACT; an added benefit is therefore not proven.

2.5.3 Probability and extent of added benefit (research question 3)

The present research question was not subject of the company's benefit assessment; so the content of the dossier was incomplete. Irrespective of this, the Institute's search identified no RCT of direct comparison on research question 3. Overall, an added benefit of dapagliflozin plus one other blood-glucose lowering drug except insulin and metformin for adults with type 2 diabetes mellitus in comparison with the ACT is not proven.

2.5.4 List of included studies (research question 3)

Not applicable as the company presented no relevant data for the benefit assessment.

2.6 Research question 4: dapagliflozin plus at least 2 other blood-glucose lowering drugs except insulin

2.6.1 Information retrieval and study pool (research question 4)

The company did not investigate the present research question in its benefit assessment.

To check whether there are RCTs of direct comparison for research question 4, a search on dapagliflozin was conducted in the trial registries ClinicalTrials.gov, ICTRP Search Portal, EU Clinical Trials Register, and PharmNet.Bund – Klinische Prüfungen (last search on 16 July 2019).

No relevant study was identified from the check.

2.6.2 Results on added benefit (research question 4)

The company did not investigate the research question in its benefit assessment, and hence did not present any data for the assessment of the added benefit of dapagliflozin in comparison with the ACT. This resulted in no hint of an added benefit of dapagliflozin plus at least 2 other blood-glucose lowering drugs except insulin for adults with type 2 diabetes mellitus in comparison with the ACT; an added benefit is therefore not proven.

2.6.3 Probability and extent of added benefit (research question 4)

The present research question was not subject of the company's benefit assessment; so the content of the dossier was incomplete. Irrespective of this, the Institute's search identified no RCT of direct comparison on research question 4. Overall, an added benefit of dapagliflozin plus at least 2 other blood-glucose lowering drugs except insulin for adults with type 2 diabetes mellitus in comparison with the ACT is not proven.

2.6.4 List of included studies (research question 4)

Not applicable as the company presented no relevant data for the benefit assessment.

2.7 Research question 5: dapagliflozin plus insulin (without or with one other blood-glucose lowering drug)

2.7.1 Information retrieval and study pool (research question 5)

The company did not investigate the present research question in its benefit assessment.

To check whether there are RCTs of direct comparison for research question 5, a search on dapagliflozin was conducted in the trial registries ClinicalTrials.gov, ICTRP Search Portal, EU Clinical Trials Register, and PharmNet.Bund – Klinische Prüfungen (last search on 16 July 2019).

No relevant study was identified from the check.

2.7.2 Results on added benefit (research question 5)

The company did not investigate the research question in its benefit assessment, and hence did not present any data for the assessment of the added benefit of dapagliflozin in comparison with the ACT. This resulted in no hint of an added benefit of dapagliflozin plus insulin (without or with one other blood-glucose lowering drug) for adults with type 2 diabetes mellitus in comparison with the ACT; an added benefit is therefore not proven.

2.7.3 Probability and extent of added benefit (research question 5)

The present research question was not subject of the company's benefit assessment; so the content of the dossier was incomplete. Irrespective of this, the Institute's search identified no RCT of direct comparison on research question 5. Overall, an added benefit of dapagliflozin

plus insulin (without or with one other blood-glucose lowering drug) for adults with type 2 diabetes mellitus in comparison with the ACT is not proven.

2.7.4 List of included studies (research question 5)

Not applicable as the company presented no relevant data for the benefit assessment.

2.8 Probability and extent of added benefit – summary

Table 5: Dapagliflozin – probability and extent of added benefit

Research question	Subindication[a]	ACT[b]	Probability and extent of added benefit
1	Monotherapy when diet and exercise alone do not provide adequate glycaemic control and the use of metformin is considered inappropriate due to intolerance	▪ Sulfonylurea (glibenclamide or glimepiride)	Added benefit not proven
2	Combination with one other blood-glucose lowering drug (except insulin, here metformin), when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Metformin + sulfonylurea (glibenclamide or glimepiride) or ▪ metformin + empagliflozin or ▪ metformin + liraglutide[c]	Added benefit not proven
3	Combination with one other blood-glucose lowering drug (except insulin and metformin), when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Metformin + sulfonylurea (glibenclamide or glimepiride) or ▪ metformin + empagliflozin or ▪ metformin + liraglutide[c] or ▪ human insulin if metformin is not tolerated or contraindicated according to the SPC	Added benefit not proven
4	Combination with at least 2 other blood-glucose lowering drugs (except insulin), when these, together with diet and exercise, do not provide adequate glycaemic control	▪ Human insulin + metformin or ▪ human insulin + empagliflozin[c] or ▪ human insulin + liraglutide[c] or ▪ human insulin if, according to the SPC, the specified combination partners are not tolerated, contraindicated or not sufficiently effective due to advanced type 2 diabetes mellitus	Added benefit not proven
5	Combination with insulin, without or with one other blood-glucose lowering drug, when this, together with diet and exercise, does not provide adequate glycaemic control	▪ Optimization of the human insulin regimen (if applicable + metformin or empagliflozin[c] or liraglutide[c])	Added benefit not proven

a: Subdivisions of the therapeutic indication according to the G-BA.
b: Presentation of the respective ACT specified by the G-BA.
c: Empagliflozin or liraglutide, each in combination with other medication for the treatment of cardiovascular risk factors, in particular antihypertensive medications, anticoagulants and/or lipid-lowering drugs, and only for patients with manifest cardiovascular disease (for the operationalization, see inclusion criteria of the relevant studies for empagliflozin [1] and liraglutide [2]).
ACT: appropriate comparator therapy; G-BA: Federal Joint Committee; SPC: Summary of Product Characteristics

The assessment described above deviates from that of the company, which did not investigate the research questions mentioned above in its benefit assessment.

The G-BA decides on the added benefit.

References for English extract

Please see full dossier assessment for full reference list.

The reference list contains citations provided by the company in which bibliographical information may be missing.

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The full report (German version) is published under https://www.iqwig.de/en/projects-results/projects/drug-assessment/a19-53-dapagliflozin-type-2-diabetes-mellitus-benefit-assessment-according-to-35a-social-code-book-v.12452.html.