Midostaurin
(systemic mastocytosis)

Benefit assessment according to §35a SGB V[1]

EXTRACT

Project: A23-111 Version: 1.0 Status: 9 Feb 2024 DOI: 10.60584/A23-111_en

[1] Translation of Sections I 1 to I 6 of the dossier assessment *Midostaurin (akute myeloische Leukämie) – Nutzenbewertung gemäß § 35a SGB V*. 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.

Publishing details

Publisher

Institute for Quality and Efficiency in Health Care

Topic

Midostaurin (systemic mastocytosis) – Benefit assessment according to §35a SGB V

Commissioning agency

Federal Joint Committee

Commission awarded on

14 November 2023

Internal Project No.

A23-111

DOI-URL

https://doi.org/10.60584/A23-111_en

Address of publisher

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
Im Mediapark 8
50670 Köln
Germany

Phone: +49 221 35685-0
Fax: +49 221 35685-1
E-mail: berichte@iqwig.de
Internet: www.iqwig.de

Medical and scientific advice

No advisor on medical and scientific questions was available for the present dossier assessment.

Patient and family involvement

The questionnaire on the disease and its treatment was answered by Nicole Hegmann.

IQWiG thanks the respondent and Mastozytose Selbsthilfe Netzwerk e. V. for participating in the written exchange and for their support. The respondent and Mastozytose Selbsthilfe Netzwerk e. V. were not involved in the actual preparation of the dossier assessment.

IQWiG employees involved in the dossier assessment

- Michael Köhler
- Benjamin Becker
- Claudia Kapp
- Philip Kranz
- Mandy Kromp
- Christopher Kunigkeit
- Regine Potthast
- Veronika Schneck

Keywords

Midostaurin, Mastocytosis – Systemic, Benefit Assessment

Part I: Benefit assessment

I Table of contents

I List of tables[2]

Page

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

I List of abbreviations

Abbreviation	Meaning
AHN	associated haematologic neoplasm
ASM	aggressive systemic mastocytosis
ACT	appropriate comparator therapy
AdvSM	advanced systemic mastocytosis
BSC	best supportive care
G-BA	Gemeinsamer Bundesausschuss (Federal Joint Committee)
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen (Institute for Quality and Efficiency in Health Care)
MCL	mast cell leukaemia
RCT	randomized controlled trial
SGB	Social Code Book V
SM-AHN	systemic mastocytosis with associated haematologic neoplasm

I 1 Executive summary of the benefit assessment

Background

In accordance with § 35a Social Code Book (SGB) V, the Federal Joint Committee (G-BA) has commissioned the Institute for Quality and Efficiency in Health Care (IQWiG) to assess the benefit of the drug midostaurin. The assessment is based on a dossier compiled by the pharmaceutical company (hereinafter referred to as the "company"). The dossier was sent to IQWiG on 14 November 2023.

Research question

The aim of this report is to assess the added benefit of midostaurin compared with the appropriate comparator therapy (ACT) in adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematologic neoplasm (SM-AHN), or mast cell leukaemia (MCL).

The research question presented in Table 2 is derived from the ACT specified by the G-BA.

Table 2: Research question for the benefit assessment of midostaurin

Therapeutic indication	**ACT**[a]
Adult patients with aggressive systemic mastocytosis, systemic mastocytosis with associated haematologic neoplasm, or mast cell leukaemia	Individualized treatment[b] selected[b] from: ▪ avapritinib (only for patients after at least one prior systemic therapy and with platelet counts ≥ 50 x 109/l), ▪ cladribined and ▪ imatinib (only for patients without KIT D816V mutation or with unknown KIT mutation status and for patients with existing eosinophilia with FIP1L1-PDGFRα fusion gene), taking into account the general condition, KIT mutation status and previous therapy

a. Presented is the ACT specified by the G-BA.
b. According to the G-BA, it is assumed that cytoreductive therapy is indicated for patients in the present therapeutic indication and that stem cell transplantation is not an option at the time of treatment with midostaurin. According to the G-BA, it is assumed that patients with SM-AHN will receive treatment for the associated haematologic neoplasm in accordance with the generally accepted state of medical knowledge, if indicated. According to the G-BA, it is expected that patients in both study arms will have access to adequate treatment to alleviate mediator-related symptoms if required, even when receiving cytoreductive therapy, which may include the use of H1 and H2 receptor antagonists, leukotriene antagonists, cromoglicic acid, corticosteroids, proton pump inhibitors, omalizumab, epinephrine, bisphosphonates and other drugs, depending on the symptoms.
c. For the implementation of individualized therapy in a direct comparative study, according to the G-BA, the investigator is expected to have a selection of several treatment options at disposal to permit an individualized treatment decision taking into account the listed criteria (multicomparator study). A rationale must be provided for the choice and any limitation of treatment options. The decision on individualized treatment with regard to the comparator therapy should be made before group allocation (e.g. randomization). If only a single-comparator study is submitted, the extent to which conclusions on a subpopulation can be derived will be examined as part of the benefit assessment.
d. The following drugs recommended in this NCCN guideline are not approved for the present therapeutic indication: cladribine and imatinib. According to the G-BA, evidence has shown that cladribine is a relevant treatment option for patients if, for example, a rapid reduction in the disease burden is required. According to the G-BA, evidence has shown that imatinib is a treatment option for patients without a KIT D816V mutation or with unknown KIT mutation status and for patients with existing eosinophilia with FIP1L1-PDGFRα fusion gene.

FIP1L1-PDGFRα: FIP1-like1-platelet-derived growth factor receptor α; G-BA: Joint Federal Committee; H1 receptor: histamine 1 receptor; H2 receptor: histamine 2 receptor; NCCN: National Comprehensive Cancer Network

On 28 November 2023, 2 months after the company had submitted the dossier (14 November 2023), the G-BA modified the ACT as shown in Table 2. In addition to the drugs listed in Table 2, the original ACT of 21 December 2022 also included best supportive care (BSC) as a suitable treatment option that would have had to be considered in the context of individualized treatment.

The company's information in the dossier refers to the original ACT of 21 December 2022. This had no consequences for the present benefit assessment, as the company did not present

suitable evidence for deriving an added benefit for any of the ACTs mentioned. The benefit assessment is based on the adjusted ACT of 28 November 2023.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

Results

Evidence provided by the company

No relevant randomized controlled trials (RCTs) for the direct comparison of midostaurin versus the ACT specified by the G-BA were identified. In its assessment, the company included the label-enabling studies D2201 and A2213 on the one hand, and the non-randomized retrospective comparative study Lübke 2022 on the other. None of these studies is suitable for the benefit assessment. This is explained below.

Single-arm studies D2201 and A2213

Studies D2201 and A2213 are single-arm phase 2 studies with midostaurin for the treatment of adults with ASM or MCL, each with or without AHN. In both studies, midostaurin was administered at a dose of 100 mg twice daily as specified in the Summary of Product Characteristics (SPC). Primary outcome of both studies was the objective response rate. As the two single-arm studies D2201 and A2213 did not allow a comparison with the ACT specified by the G-BA, they are unsuitable for assessing an added benefit of midostaurin.

Non-randomized retrospective comparative study Lübke 2022

The publication Lübke 2022 describes a non-randomized retrospective comparative study that was conducted using data from the German Register of Eosinophil and Mast Cell Diseases. Patients were treated with either midostaurin or cladribine, either as a single treatment or as sequential administration of these two drugs. The dosage of midostaurin was 100 mg twice daily, which corresponds to the information in the SPC. Cladribine was administered subcutaneously or intravenously at 0.14 mg/kg/day on Days 1 to 5 of a 28-day cycle. Among other things, the outcomes considered included overall survival, leukaemia-free survival and event-free survival. The company based its derivation of the added benefit on the two cohorts that were treated exclusively with midostaurin or cladribine.

The registry study described in Lübke 2022 is not suitable for deriving an added benefit of midostaurin. All patients in the comparator group were treated exclusively with cladribine. However, the ACT provides for an individualized treatment under consideration of avapratinib, cladribine and imatinib. The data in Module 4B and the publication Lübke 2022 provide no information on whether cladribine is the most suitable individualized treatment for all patients in the comparator group. Furthermore, this is a non-randomized comparison. The publication and Module 4B mention that a propensity score analysis was performed to

account for differences in demographic and disease-related characteristics between patients receiving midostaurin and cladribine. However, the methods for the propensity score procedure used are not sufficiently described either in Module 4B or in the Lübke 2022 publication.

For the non-randomized comparison in the Lübke 2022 study, it is therefore overall unclear whether adequate methods were used to establish structural equality. Therefore, the results on the outcomes reported in Module 4B were not used for the benefit assessment. Irrespective of the company's approach, there are no effects in the present scenario for which it can be ruled out with sufficient certainty that they result solely from systematic bias due to confounders.

Results on added benefit

No suitable data are available for the assessment of the added benefit of midostaurin for the treatment of adults with ASM, SM-AHN or MCL compared with the ACT. There is no hint of an added benefit of midostaurin in comparison with the ACT; an added benefit is therefore not proven.

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

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

Table 3: Midostaurin – probability and extent of added benefit

Therapeutic indication	ACT[a]	Probability and extent of added benefit
Adult patients with ASM, SM-AHN or MCL	Individualized treatment choosing from ▪ avapritinib (only for patients after at least one prior systemic therapy and with platelet counts ≥ 50 x 109/l), ▪ cladribine and ▪ imatinib (only for patients without KIT D816V mutation or with unknown KIT mutation status and for patients with existing eosinophilia with FIP1L1-PDGFRα fusion gene) taking into account the general condition, KIT mutation status and previous therapy	Added benefit not proven
a. Presented is the ACT specified by the G-BA. FIP1L1-PDGFRα: FIP1-like1-Platelet-Derived Growth Factor Receptor α; G-BA: Federal Joint Committee; HES: hypereosinophilic syndrome		

The G-BA decides on the added benefit.

Supplementary note

The result of the assessment deviates from the result of the G-BA's assessment in the context of the market launch in 2017, where the G-BA had determined a non-quantifiable added benefit of midostaurin. However, in this assessment, the added benefit had been regarded as proven by the approval irrespective of the underlying data because of the special situation for orphan drugs.

I 2 Research question

The aim of this report is to assess the added benefit of midostaurin compared with the ACT in adult patients with ASM, SM-AHN or MCL.

The research question presented in Table 4 is derived from the ACT specified by the G-BA.

Table 4: Research question for the benefit assessment of midostaurin

Therapeutic indication	**ACT[a]**
Adult patients with ASM, SM-AHN or MCL	Individualized treatment[b] selectedb from: ▪ avapritinib (only for patients after at least one prior systemic therapy and with platelet counts ≥ 50 x 109/l), ▪ cladribined and ▪ imatinib (only for patients without KIT D816V mutation or with unknown KIT mutation status and for patients with existing eosinophilia with FIP1L1-PDGFRα fusion gene), taking into account the general condition, KIT mutation status and previous therapy

a. Presented is the ACT specified by the G-BA.
b. According to the G-BA, it is assumed that cytoreductive therapy is indicated for patients in the present therapeutic indication and that stem cell transplantation is not an option at the time of treatment with midostaurin. According to the G-BA, it is assumed that patients with SM-AHN will receive treatment for the associated haematologic neoplasm in accordance with the generally accepted state of medical knowledge, if indicated. According to the G-BA, it is expected that patients in both study arms will have access to adequate treatment to alleviate mediator-related symptoms if required, even when receiving cytoreductive therapy, which may include the use of H1 and H2 receptor antagonists, leukotriene antagonists, cromoglicic acid, corticosteroids, proton pump inhibitors, omalizumab, epinephrine, bisphosphonates and other drugs, depending on the symptoms.
c. For the implementation of individualized therapy in a direct comparative study, according to the G-BA, the investigator is expected to have a selection of several treatment options at disposal to permit an individualized treatment decision taking into account the listed criteria (multicomparator study). A rationale must be provided for the choice and any limitation of treatment options. The decision on individualized treatment with regard to the comparator therapy should be made before group allocation (e.g. randomization). If only a single-comparator study is submitted, the extent to which conclusions on a subpopulation can be derived will be examined as part of the benefit assessment.
d. The following drugs recommended in this NCCN guideline are not approved for the present therapeutic indication: cladribine and imatinib. According to the G-BA, evidence has shown that cladribine is a relevant treatment option for patients if, for example, a rapid reduction in the disease burden is required. According to the G-BA, evidence has shown that imatinib is a treatment option for patients without a KIT D816V mutation or with unknown KIT mutation status and for patients with existing eosinophilia with FIP1L1-PDGFRα fusion gene.

FIP1L1-PDGFRα: FIP1-like1-platelet-derived growth factor receptor α; G-BA: Joint Federal Committee; H1 receptor: histamine 1 receptor; H2 receptor: histamine 2 receptor; NCCN: National Comprehensive Cancer Network

On 28 November 2023, 2 months after the company had submitted the dossier (14 November 2023), the G-BA modified the ACT as shown in Table 4. In addition to the drugs listed in Table 4,

the original ACT of 21 December 2022 also included BSC as a suitable treatment option that would have had to be considered in the context of individualized treatment.

The company's information in the dossier refers to the original ACT of 21 December 2022. This had no consequences for the present benefit assessment, as the company did not present suitable evidence for deriving an added benefit for any of the ACTs mentioned (see Chapter I 3). The benefit assessment is based on the adjusted ACT of 28 November 2023.

The assessment was conducted by means of patient-relevant outcomes on the basis of the data provided by the company in the dossier.

I 3 Information retrieval and study pool

The study pool of the assessment was compiled on the basis of the following information:

Sources of the company in the dossier:

- study list on midostaurin (status: 16 August 2023)
- bibliographical literature search on midostaurin (last search on 16 August 2023)
- search in trial registries/trial results databases for studies on midostaurin (last search on 22 August 2023)
- search on the G-BA website for midostaurin (last search on 22 August 2023)

To check the completeness of the study pool:

- search in trial registries for studies on midostaurin (last search on 30 November 2023); for search strategies, see I Appendix A of the full dossier assessment.

Direct comparison

The check for completeness of the study pool identified no relevant RCTs on the direct comparison of midostaurin versus the G-BA's ACT. This concurs with the company's assessment.

Further investigations

The company identified no RCT permitting a direct comparison or an adjusted indirect comparison using a common comparator of midostaurin versus the ACT. It therefore also conducted an information retrieval on further investigations with midostaurin. The company identified the two single-arm studies CPKC412D2201 [1-3] (hereinafter referred to as D2201) and CPKC412A2213 [4] (hereinafter referred to as A2213), on the basis of which midostaurin was approved. The company conducted no information retrieval on other investigations with the ACT.

Furthermore, the company stated that the non-randomized retrospective comparative study Lübke 2022 [5] should be included and presented as supplementary information. The study compared midostaurin with cladribine in patients with ASM, SM-AHN or MCL. It also used this study to derive an added benefit. It cannot be inferred from the information in Module 4B how the company identified this study or whether it was identified via a systematic literature search. The study is a retrospective data analysis, a study type that the company excluded in its inclusion criteria for non-randomized studies.

A check of the completeness of the study pool presented by the company for the other investigations was foregone because the data submitted by the company were not suitable

for drawing conclusions on the added benefit of midostaurin in the present therapeutic indication due to a missing or unsuitable comparator therapy. This is explained below.

Evidence presented by the company

In its assessment, the company included the label-enabling studies D2201 and A2213 on the one hand, and the non-randomized retrospective comparative study Lübke 2022 on the other.

Single-arm studies D2201 and A2213

The studies D2201 and A2213 are single-arm phase 2 studies with midostaurin.

Study D2201 included patients with ASM or MCL (with or without AHN) who met the World Health Organization (WHO) diagnostic criteria and also had at least 1 measurable C-finding (organ damage typical of advanced SM, e.g. cytopenias, hypalbuminaemia, portal hypertension, malabsorption [6]) [7,8]. Patients with MCL also had to have at least 20% immature mast cells in the bone marrow aspirate. In patients with AHN, this component of the disease was not allowed to be acute or life-threatening. The total of 116 patients received midostaurin at a dose of 100 mg twice daily, continuously in cycles of 28 days until death, disease progression or the occurrence of unacceptable toxicity. This dosage corresponds to the specifications of the SPC [9]. The study was to be terminated 5 years after the first treatment of the last patient or when all patients had discontinued the study treatment, whichever occurred first. Primary outcome of the study was the objective response rate.

Patients with histologically documented ASM or MCL (each with or without AHN) were included in study A2213. C-findings were not recorded at study inclusion. A total of 26 patients were treated continuously with midostaurin at a dose of 100 mg twice daily for a maximum of 12 cycles of 28 days each but could also receive midostaurin beyond this in an extension phase. This dosage corresponds to the specifications of the SPC [9]. If there was no response to the therapy after 2 cycles, treatment was discontinued. Primary outcome of the study was the objective response rate.

As the single-arm studies D2201 and A2213 study did not allow a comparison with the ACT specified by the G-BA, they are unsuitable for assessing an added benefit of midostaurin.

Non-randomized retrospective comparative study Lübke 2022

The publication Lübke 2022 describes a non-randomized retrospective comparative study that was conducted using data from the German Register of Eosinophil and Mast Cell Diseases. A total of 139 patients with advanced systemic mastocytosis (AdvSM) who were enrolled in the registry between 2003 and 2020 were included. Among the 139 patients, there were 22 patients with ASM (15.8%), 92 with SM-AHN (66.2%) and 25 with MCL (18.0 %). Diagnosis and classification into the respective subtypes of the disease was made according to the criteria of the World Health Organisation (WHO) from 2017 [10]. Patients were treated with either

midostaurin or cladribine, either as a single treatment or as sequential administration of these two drugs. The dosage of midostaurin was 100 mg twice daily, which corresponds to the specification in the SPC [9]. Adjustments were made depending on efficacy and tolerability, but these are not described in detail in the publication. Cladribine was administered subcutaneously or intravenously at 0.14 mg/kg/day on Days 1 to 5 of a 28-day cycle. The median treatment duration for patients treated with cladribine was 3 cycles (range: 1 to 8 cycles). This corresponds to the information in the German Society of Haematology and Oncology (DGHO) guideline [6]. Among other things, the outcomes considered included overall survival, leukaemia-free survival and event-free survival. 63 (45.3%) patients received exclusively midostaurin, 23 (16.5%) received exclusively cladibrine, 30 (21.6%) received midostaurin followed by cladribine and 23 (16.5%) patients received cladribine followed by midostaurin. The company based its derivation of the added benefit on the two cohorts that were treated exclusively with midostaurin or cladribine.

The registry study described in Lübke 2022 is not suitable for deriving an added benefit of midostaurin. All patients in the comparator group were treated exclusively with cladribine. However, the ACT provides for an individualized treatment under consideration of avapratinib, cladribine and imatinib. The data in Module 4B and the publication Lübke 2022 provide no information on whether cladribine is the most suitable individualized treatment for all patients in the comparator group. Furthermore, this is a non-randomized comparison. Since the necessary structural equality between the treatment groups is not guaranteed in non-randomized studies, group differences in possible confounders, i.e. factors that are related to both the treatment and outcomes and can thus alter a treatment effect, must be taken into account in the effect estimation. The first prerequisite for this is that relevant confounders are systematically identified. Then it must be ensured that the dataset used contains the necessary information on the identified confounders so that they can be adjusted using suitable methods (e.g. propensity score matching).

It is not clear from the information in the Lübke 2022 publication that the conditions described above were met in the study. There is a lack of information on the identification and completeness of the confounders in the data set used. For the adjustment, the publication Lübke 2022 and Module 4B only describe that a propensity score analysis was performed with the variables age, haemoglobin, platelets and presence of an S/A/R mutation (variables of the mutation-adjusted risk score [MARS] [11]) to account for differences in demographic and disease-related characteristics between patients receiving midostaurin and cladribine. Therefore, the identification and completeness of confounders and the adjustment made for them are not described in Module 4B or in the Lübke 2022 publication in a way that allows the different steps to be adequately understood. The company also presents no protocol for the study. For the non-randomized comparison in the Lübke 2022 study, it is therefore unclear whether adequate methods were used to establish structural equality. Therefore, the results

on the outcomes reported in Module 4B were not used for the benefit assessment. Irrespective of the company's approach, there are no effects in the present scenario for which it can be ruled out with sufficient certainty that they result solely from systematic bias due to confounders.

Summary

To derive the added benefit of midostaurin, the company included 2 single-arm studies and a non-randomized retrospective analysis. None of these studies was suitable for the benefit assessment. Overall, the company has therefore presented no suitable data for deriving an added benefit in comparison with the ACT.

I 4 Results on added benefit

No suitable data are available for the assessment of the added benefit of midostaurin for the treatment of adults with ASM, SM-AHN or MCL compared with the ACT. There is no hint of an added benefit of midostaurin in comparison with the ACT; an added benefit is therefore not proven.

I 5 Probability and extent of added benefit

The result of the assessment of the added benefit of risdiplam in comparison with the ACT is summarized in Table 5.

Table 5: Midostaurin – probability and extent of added benefit

Therapeutic indication	**ACT[a]**	**Probability and extent of added benefit**
Adult patients with ASM, SM-AHN or MCL	Individualized treatment choosing from ▪ avapritinib (only for patients after at least one prior systemic therapy and with platelet counts ≥ 50 x 109/l), ▪ cladribine and ▪ imatinib (only for patients without KIT D816V mutation or with unknown KIT mutation status and for patients with existing eosinophilia with FIP1L1-PDGFRα fusion gene) taking into account the general condition, KIT mutation status and previous therapy	Added benefit not proven
a. Presented is the ACT specified by the G-BA. FIP1L1-PDGFRα: FIP1-like1-Platelet-Derived Growth Factor Receptor α; G-BA: Federal Joint Committee; HES: hypereosinophilic syndrome		

The assessment described above deviates from that of the company, which derived a hint of a non-quantifiable added benefit for midostaurin.

The G-BA decides on the added benefit.

Supplementary note

The result of the assessment deviates from the result of the G-BA's assessment in the context of the market launch in 2017, where the G-BA had determined a non-quantifiable added benefit of midostaurin. However, in this assessment, the added benefit had been regarded as proven by the approval irrespective of the underlying data because of the special situation for orphan drugs.

I 6 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.

1. Gotlib J, Kluin-Nelemans HC, George TI et al. Efficacy and Safety of Midostaurin in Advanced Systemic Mastocytosis. N Engl J Med 2016; 374(26): 2530-2541. https://doi.org/10.1056/NEJMoa1513098.

2. Hartmann K, Gotlib J, Akin C et al. Midostaurin improves quality of life and mediator-related symptoms in advanced systemic mastocytosis. The Journal of allergy and clinical immunology 2020; 146(2): 356-366.e4. https://doi.org/10.1016/j.jaci.2020.03.044.

3. Jawhar M, Schwaab J, Naumann N et al. Response and progression on midostaurin in advanced systemic mastocytosis: KIT D816V and other molecular markers. Blood 2017; 130(2): 137-145. https://doi.org/10.1182/blood-2017-01-764423.

4. DeAngelo DJ, George TI, Linder A et al. Efficacy and safety of midostaurin in patients with advanced systemic mastocytosis: 10-year median follow-up of a phase II trial. Leukemia 2018; (32): 470-478. https://doi.org/10.1038/leu.2017.234.

5. Lubke J, Schwaab J, Naumann N et al. Superior Efficacy of Midostaurin Over Cladribine in Advanced Systemic Mastocytosis: A Registry-Based Analysis. J Clin Oncol 2022; 40(16): 1783-1794. https://doi.org/10.1200/JCO.21.01849.

6. Reiter A, Jawhar M, Balabanov S et al. Onkopedia Leitlinien - Mastozytose, systemische [online]. 2020. URL: https://www.onkopedia.com/de/onkopedia/guidelines/mastozytose-systemische/@@guideline/html/index.html.

7. Valent P, Horny HP, Escribano L et al. Diagnostic criteria and classification of mastocytosis: a consensus proposal. Leuk Res 2001; 25(7): 603-625.

8. Valent P, Akin C, Sperr WR et al. Aggressive systemic mastocytosis and related mast cell disorders: current treatment options and proposed response criteria. Leuk Res 2003; 27(7): 635-641.

9. Novartis Pharma. Rydapt 25 mg Weichkapseln [online]. 2023 [Accessed: 19.01.2024]. URL: https://www.fachinfo.de.

10. Horny HP, Akin C, Arber DA et al. Mastocytosis (mast cell disease). In: Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H und Thiele J (Hg.): WHO classification of tumours of haematopoietic and lymphoid tissues. Revised 4th edition. Lyon: International Agency for Research on Cancer (World Health Organization classification of tumours), 2017; 62–69.

11. Jawhar M, Schwaab J, Alvarez-Twose I et al. MARS: Mutation-Adjusted Risk Score for Advanced Systemic Mastocytosis. J Clin Oncol 2019; 37(31): 2846-2856. https://doi.org/10.1200/JCO.19.00640.

The full report (German version) is published under https://www.iqwig.de/en/projects/a23-111.html.