HAUTE AUTORITÉ DE SANTÉ

**The legally binding text is the original French version**

# TRANSPARENCY COMMITTEE

## Opinion

## 9 January 2013

## VOTRIENT 200 mg, Film-coated tablet

**B/30 (CIP code: 491 313 4)**

## VOTRIENT 400 mg, Film-coated tablet

**B/30 (CIP code: 491 315 7)**

## VOTRIENT 400 mg, Film-coated tablet

**B/60 (CIP code: 491 316 3)**

Applicant: GlaxoSmithKline

| | |
|---|---|
| INN | Pazopanib |
| ATC code (2011) | L01XE (Protein kinase inhibitors) |
| Reason for the review | **Inclusion for an extension of indication** |
| List(s) concerned | **National Health Insurance** (French Social Security Code L.162-17)<br>**Hospital use** (French Public Health Code L.5123-2) |
| Indication(s) concerned | **"VOTRIENT is indicated for the treatment of adult patients with selective subtypes of advanced soft tissue sarcoma (STS) who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy".** |

| | |
|---|---|
| **Actual Benefit** | The actual benefit of VOTRIENT is substantial in this indication. |
| **Improvement in Actual Benefit** | VOTRIENT has a minor IAB (level IV) in terms of efficacy compared with the current treatment strategy. |
| **Therapeutic use** | VOTRIENT is an alternative treatment for the management of patients suffering from metastatic soft tissue sarcoma, excluding liposarcoma and GIST, when treatment with anthracyclines or ifosfamide has failed. |

# 01 ADMINISTRATIVE AND REGULATORY INFORMATION

| | |
|---|---|
| Marketing Authorisation (Centralised European) | Date of Marketing Authorisation (centralised procedure): 14 June 2010<br>Amendment of 3 August 2012 |
| Prescribing and dispensing conditions/special status | List I<br>Medicinal product reserved for hospital use. Prescription restricted to oncology or haematology specialists or doctors with cancer training.<br>Medicinal product requiring special monitoring during treatment. |

| | |
|---|---|
| ATC Classification | 2011<br>L : Antineoplastic and immunomodulating agents<br>L01 : Antineoplastic agents<br>L01X : Other antineoplastic agents<br>L01XE : Protein kinase inhibitors<br>L01XE11 : Pazopanib |

# 02 THERAPEUTIC INDICATION(S)

*"Renal Cell Carcinoma - RCC*

VOTRIENT is indicated for adults for the first line treatment of advanced renal cell carcinoma (RCC) and for patients who have received prior cytokine therapy for advanced disease.

***Soft tissue sarcoma - STS***

**VOTRIENT is indicated for the treatment of adult patients with selective subtypes of advanced soft tissue sarcoma (STS) who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy.**
**Efficacy and safety has only been established in certain STS histological tumour subtypes (see section 5.1 of the SPC).**"

# 03 DOSAGE

"Adults
The recommended dose of pazopanib for the treatment of RCC or STS is 800 mg once daily.

Dose modifications
Dose modification should be in 200 mg increments in a step-wise fashion based on individual tolerability in order to manage adverse reactions. The dose of pazopanib should not exceed 800 mg."

# 04 THERAPEUTIC NEED[1,2]

Soft tissue sarcomas (STS) are rare diseases (less than 1% of all malignant conditions in adults). They are a heterogeneous group of connective tissue cancers arising from mesenchymal cells and their precursors. There are several histopathological subtypes of STS.

- Treatment for local diseases is based mainly on surgery and radiotherapy. Control of the primary tumour and local relapses prevention firstly require full surgical resection, which must also be intended to preserve function. The role of adjuvant chemotherapy is controversial.
- In metastatic disease, the treatment is based on systemic chemotherapy. Soft tissue sarcomas are relatively poorly chemosensitive and a limited number of effective molecules are available for them: the anthracyclines, mostly doxorubicin, ifosfamide and dacarbazine. These compounds are used alone or in combination in the metastatic phase of the disease; in first line treatment, the percentage of response rates range from 20 to 40% with median survival periods of 12 to 18 months.

Many randomised studies have established that:

- the combinations without anthracyclines are less effective than doxorubicin alone.
- for equivalent doses of doxorubicin, adding a second compound produces occasionally superior response rates but at the cost of greater toxicity and without changing survival.
- sensitivity to chemotherapy varies depending on the histological subtypes: synovial sarcomas are specifically sensitive to ifosfamide, undifferentiated liposarcomas are the most chemosensitive, leiomyosarcomas are particularly sensitive to the combination of gemcitabine and docetaxel and angiosarcomas are particularly sensitive to weekly paclitaxel.

After failure to treatment including doxorubicin and ifosfamide in monotherapy or in combination, trabectedine has Marketing Authorisation only for liposarcomas or leiomyosarcomas.

[1] Italiano A, Mathoulin-Pelissier S, Le Cesne A, Terrier P, Bonvalot S, Collin F, Michels JJ, Blay JY, Coindre JM and Bui B. Trends in Survival for Patients With Metastatic Soft-Tissue Sarcoma. Cancer 2011; 117:1049–54.

[2] Le Cesne A, Cioffi A. Chimiothérapie des sarcomes des tissus mous métastatiques et localement avancés. Oncol. 2007; 9 (2): 114-125.

# 05 CLINICALLY RELEVANT COMPARATORS

## 05.1 Medicinal products

No alternative medicinal products have Marketing Authorisation for the current indication for VOTRIENT.
YONDELIS from the PHARMA MAR company has joint Marketing Authorisation with VOTRIENT only in the histological subgroup of leiomyosarcoma.
*- YONDELIS (trabectedine) 0.25 mg and 1 mg, powder for concentrate for solution for infusion, indicated for the treatment of adult patients with advanced soft tissue sarcoma, after failure of anthracyclines and ifosfamide, or who are unsuited to receive these agents. . The efficacy data are based mainlyon liposarcoma and leiomyosarcoma patients (2007 Marketing Authorisation).*
Data on the therapeutic benefit of YONDELIS in this indication are obtained from a non-comparative phase II study.

### ◗ Conclusion

**There is no clinically relevant comparator for VOTRIENT.**

# 06 INTERNATIONAL INFORMATION ON THE MEDICINAL PRODUCT

| Country | REIMBURSED | |
|---|---|---|
| | YES/NO<br>If no, why | Population(s)<br>Marketing Authorisation or restricted population |
| USA | Yes | Marketing Authorisation population in sarcoma |
| EU | Ongoing assessment in sarcoma | |

# 07 ANALYSIS OF AVAILABLE DATA

The application file for registration includes:

- a non-comparative phase II study (study VEG20002),
- a pivotal, placebo-controlled phase III study (study VEG110727)

## 07.1 Efficacy

**Study VEG20002**

This was a non-comparative phase II study designed to evaluate the efficacy and safety of VOTRIENT (pazopanib) in patients with one of the four types of soft tissue sarcomas most frequently seen in the EORTC database (leiomyosarcoma, liposarcoma, synovial sarcoma and fibrosarcoma), in relapse after standard treatment or for which no standard treatment is available.

The patients were treated with VOTRIENT at a dose of 800 mg per day orally until disease progression, death, development of unacceptable adverse effects due to the substance, intercurrent disease or withdrawal of patient consent.

The primary efficacy endpoint was the non-progression rate (which included complete and partial responses and stable disease) at 12 weeks from a CT scan evaluation of the disease, based on RECIST criteria.

The main secondary efficacy endpoints were:

- progression-free survival, defined as the time between the date on which VOTRIENT was first administrated and the date on which disease progression or death (all causes combined) was first observed. Progression was assessed by the investigator.
- overall survival, defined as the time between the date on which VOTRIENT was first administrated and death regardless of cause.
- the response rate, defined as the percentage of patients with complete response (CR) or partial response (PR) according to the RECIST criteria, based on the investigators' evaluation.

The non-progression rates at 12 weeks and main secondary efficacy endpoints are summarised in table 1.

**Table 1: Main efficacy results from study VEG20002**

| Efficacy endpoints | Leiomyo-sarcomas N=41 | Liposarcomas N=19 | Synovial sarcomas N=37 | Other sarcomas N=41 | Total N=138 |
|---|---|---|---|---|---|
| **Non-progression rate at 12 weeks** | | | | | |
| CR+PR+SD, n (%)<br>(90% CI)<br>p-value[a] | 17 (**41**)<br>(28.4, 55.5)<br>0.003 | 5 (**26**)<br>(11.0, 47.6)<br>0.653 | 18 (**49**)<br>(34.3, 63.2)<br><0.001 | 17 (**41**)<br>(28.4, 55.5)<br>0.003 | 57 (**41**)<br>(34.2, 48.7)<br><0.001 |
| **Progression-free survival (weeks)** | | | | | |
| Median (90% CI)[b] | **17.2**<br>(12.0, 24.1) | **11.1**<br>(7.1, 11.9) | **23.4**<br>(11.7, 29.3) | **14.0**<br>(12.0, 36.3) | **12.1**<br>(12.0, 22.4) |
| **Overall survival (months)** | | | | | |
| Median (90% CI)[b] | **11.7**<br>(10.6, 17.6) | **6.5**<br>(4.2, 19.3) | **10.3**<br>(7.6, 13.2) | **9.8**<br>(7.6, 11.3) | **10.6**<br>(9.5, 11.7) |
| **Percentage overall response** | | | | | |
| CR+PR, n (%)<br>(90% CI) | 1 (**2**)<br>(0.1, 11.1) | **0**<br>(0.0, 11.4) | 4 (**11**)<br>(3.8, 23.1) | 3 (**7**)<br>(2.0, 17.8) | 8 (**6**)<br>(2.9, 10.2) |

a. p-value = level of evidence to reject the null hypothesis of a non-progression rate of 20%, with a probability of 0.10.
b. Estimates made using the Brookmeyer-Crowley method.
CR : Complete response
PR: Partial response
SD : Stable disease

The phase II study demonstrated that pazopanib had anti-tumour activity (non-progression rate at 12 weeks > 40%) in three histological groups of relapsed or refractory soft tissue sarcomas: leiomyosarcomas, synovial sarcomas and the "other sarcomas". Lack of activity in liposarcomas in this study justified the reason not to include this histological subtype in the phase III study VEG110727.

**Study VEG110727**

The efficacy and safety of pazopanib (VOTRIENT) in soft tissue sarcomas was evaluated in a double-blind, placebo-controlled, randomised, pivotal phase III study. A total of 369 patients with advanced soft tissue sarcomas were randomised to receive either pazopanib, at a dose of 800 mg once daily or placebo.

The main inclusion criteria were:

- age over 18 years old,
- metastatic soft tissue sarcoma,
- tumour progression during or within 6 months after prior treatment for advanced disease (or 12 months for patients who had only received (neo)adjuvant systemic treatment),
- the patients were required to have received treatment with anthracyclines and the usually available chemotherapies in their previous lines of treatment,
- patients could have received a maximum of four lines of prior systemic treatments for their advanced disease including a maximum of two combination regimens. These criteria did not include (neo) adjuvant and maintenance treatments,
- high grade malignant or intermediary grade tumour. Low grade tumours were also permitted if disease progression had been documented,
- measurable disease according to the solid tumour evaluation criteria (RECIST criteria v1.0),
- an initial WHO performance index of 0 or 1,
- acceptable organ function.

The non-inclusion criteria included:

- liposarcomas (all subtypes), all rhabdomyosarcomas which were neither alveolar nor pleomorphic, chondrosarcomas, osteosarcomas, Ewing's/PNET tumours, GIST, dermatofibrosarcomas protuberans, inflammatory myofibroblastic sarcomas, malignant

mesothelioma and mixed uterine mesodermal tumours.
- cerebral or leptomeningeal metastases.

The primary endpoint was progression-free survival defined as the time between the randomisation date and the first date when disease progression was recorded or death, all causes combined.
A CT scan was performed every 4 weeks until week 12, and then every 8 weeks thereafter. These were read blind on a centralised basis by independent radiologists.

The secondary endpoints were:
- overall survival, defined as the time between randomisation and death regardless of cause.
- progression-free survival in the following three histological subtypes: leiomyosarcoma, synovial sarcoma and the “other” histological types of eligible sarcomas.
- the response rate, defined as the percentage of patients whose best overall response was either a complete response (CR) or partial response (PR) according to the RECIST v1.0 criteria recorded during the period between the first dose of treatment and progression.
- the time to response, defined as the time between randomisation and the date on which CR or PR were first observed (depending on the status recorded initially).
- the duration of response, defined as the time between the date on which first CR or PR were observed and the date on which disease progression was first observed, or death regardless of cause (depending on which event occurred first).
- safety, including adverse effects, serious adverse effects and changes in vital signs from inclusion into the study including the WHO performance index, laboratory indices and the left ventricular ejection fraction.
- the patients' quality of life was also evaluated as an exploratory criterion using version 3 of the EORTC quality of life questionnaire (QLQ-C30) on admission into the study and then at weeks 4, 8 and 12. The EuroQol-5D group questionnaire (EQ-5D) was also used at inclusion into the study and at week 4.

**Results:**

A total of 369 patients were included. Median patient age was 55 years old (range: 18-83). All of the patients included were in good overall physical condition with a WHO performance index of 0 in 48% and 1 in 52%. Ninety-eight per cent (98%) of subjects had previously received an anthracycline (doxorubicin), 70% had received ifosfamide and 56% had received at least two lines of chemotherapy for advanced disease before inclusion into the study.

Median follow-up (defined as the date from randomisation to the date of last contact or death) was similar in both treatment groups (9.36 months in the placebo group and 10.04 months in the VOTRIENT group).

**Table 2: Study VEG110727, Overall efficacy results in STS**

| Endpoints/study population | VOTRIENT | Placebo | HR (95% CI) | Two-tailed p value |
|---|---|---|---|---|
| **Progression-free survival (primary endpoint)** | | | | |
| Total ITT population<br>Median (weeks) | N = 246<br>20.0 | N = 123<br>7.0 | 0.35 (0.26, 0.48) | < 0.001 |
| Leiomyosarcomas<br>Median (weeks) | N = 109<br>20.1 | N = 49<br>8.1 | 0.37 (0.23, 0.60) | < 0.001 |
| Synovial sarcomas<br>Median (weeks) | N = 25<br>17.9 | N = 13<br>4.1 | 0.43 (0.19, 0.98) | 0.005 |
| "Other STS"<br>Median (weeks) | N = 112<br>20.1 | N = 61<br>4.3 | 0.39 (0.25, 0.60) | < 0.001 |
| **Overall survival** | | | | |
| Total ITT population<br>Median (months) | N = 246<br>12.6 | N = 123<br>10.7 | 0.87 (0.67 - 1.12) | 0.256 |
| Leiomyosarcomas*<br>Median (months) | N = 109<br>16.7 | N = 49<br>14.1 | 0.84 (0.56, 1.26) | 0.363 |
| Synovial sarcomas*<br>Median (months) | N = 25<br>8.7 | N = 13<br>21.6 | 1.62 (0.79, 3.33) | 0.115 |
| "Other STS"*<br>Median (months) | N = 112<br>10.3 | N = 61<br>9.5 | 0.84 (0.59, 1.21) | 0.325 |
| **Response rate (CR + PR)** | | | | |
| %<br>[95% CI]<br>Duration of response<br>Median (weeks)<br>[95% CI] | 4<br>[2.3 - 7.9]<br><br>38.9<br>[16.7, 40.0] | 0<br>[0.0 - 3.0] | | |

HR = Hazard ratio; ITT = Intention to Treat; CR = Complete Response; PR = Partial response.

* Overall survival in the histological subgroups of the respective STS (leiomyosarcoma, synovial sarcoma and "other" STS) must be interpreted with caution because of the small number of subjects and wide confidence intervals.

Median progression-free survival (primary endpoint) was 4.6 months (20 weeks) in the VOTRIENT group compared with 1.6 months (7 weeks) in the placebo group, i.e. an absolute difference of 3 months in favour of the VOTRIENT group; the Hazard Ratio (HR) adjusted for WHO performance index and previous systemic treatment was 0.35 [0.26 – 0.48], p<0.001.
Results for the primary endpoint were consistent between the overall population and the subgroup populations. The synovial sarcoma histological subgroup, however, only contained a total of 38 patients with a very wide confidence interval of the hazard ratio and as a result the treatment effect cannot be deemed to be established in this subgroup.

Results for secondary endpoints:
The final analysis of overall survival carried out at 76% (280/369) of events showed no difference between the two treatment groups (HR=0.87, 95% CI [0.67; 1.12] p=0.256).

The response rates in the VOTRIENT and placebo groups were 4% and 0% respectively. These were all partial responses.
The median duration of response in patients who achieved a partial response in the VOTRIENT group was 38.9 weeks and the median time to response was 8.4 weeks.
There were no differences in overall quality of life score between the two groups. However, some specific symptoms such as diarrhoea, fatigue and vomiting, worsened.
No quality of life data were recorded in patients whose disease progressed or beyond the 12 week follow-up period of the study.

## 07.2 Safety/adverse effects

Treatment discontinuation due to adverse events occurred in 20% of patients in the VOTRIENT group compared with 5% in the placebo group. These events were mostly increases in ALT, dyspnoea, left ventricular dysfunction, hypertension and vomiting in the pazopanib group.
The incidence of grades 3-4 adverse events was higher in the VOTRIENT group (59%) than in the placebo group (25%). These were mostly fatigue, tumour pain, hypertension, reduced appetite, dyspnoea and diarrhoea.

## 07.3 Summary & discussion

A double-blind, randomised study has compared pazopanib (VOTRIENT) at a dosage of 800 mg/day with placebo in 369 patients suffering from metastatic soft tissue sarcoma, excluding liposarcoma and GIST (gastrointestinal stromal tumours).
All of the patients included were in good overall physical condition and 98% had previously received an anthracycline (doxorubicin), 70% had received ifosfamide and 56% had received at least two lines of prior treatment for advanced disease.
Median progression-free survival (primary endpoint) was longer with VOTRIENT than with the placebo (4.6 months compared with 1.6 months) i.e. an absolute difference of 3 months (Hazard Ratio (HR) adjusted for the WHO performance index and prior treatment was 0.35 [0.26 – 0.48]).
Results for the primary endpoint were consistent between the overall population and the subgroup populations. However, the treatment effect cannot be deemed to be established in the synovial sarcoma histological subgroup, which only contained a total of 38 patients and which had a wide confidence interval of the hazard ratio.

The final analysis of overall survival performed in 76% (280/369) of events showed no difference between pazopanib and placebo (HR=0.87, 95% CI [0.67; 1.12] p=0.256).

The response rates in the VOTRIENT and placebo groups were 4% and 0% respectively. These were all partial responses.
The overall quality of life scores for pazopanib and placebo were not different. However, some specific symptoms such as diarrhoea, fatigue and vomiting deteriorated.
No quality of life data were recorded in patients whose disease progressed or beyond the 12 week follow-up period of the study.
Treatment discontinuation due to adverse events (20% compared with 5%) and the grade 3-4 adverse events (59% compared with 25%) occurred more often with pazopanib than with placebo.
The VOTRIENT toxicity was mostly hepatic (raised ALT), gastrointestinal (vomiting, diarrhoea) and cardiovascular (hypertension, left ventricular dysfunction).

# 08 THERAPEUTIC USE [1, 2]

At the localised stage of soft tissue sarcoma, treatment mostly involves surgery and radiotherapy. Control of the primary tumour and local relapses prevention firstly require full surgical resection, which should also aim to preserve function. The role of adjuvant chemotherapy is controversial.
In metastatic disease, the treatment is based on systemic chemotherapy.
Soft tissue sarcomas are relatively poorly chemosensitive and a limited number of effective molecules are available for them: the anthracyclines, mostly doxorubicin, ifosfamide and dacarbazine. These products are used alone or in combination in the metastatic phase of the disease; in first-line treatment, the response rates range from 20 to 40% with median survival times of 12 to 18 months.
Many randomised studies have established that:

- the combinations without anthracyclines are less effective than doxorubicin alone.
- for equivalent doses of doxorubicin, adding a second compound produces occasionally superior response rates but at the cost of greater toxicity and without changing survival.
- sensitivity to chemotherapy varies depending on the histological subtypes: synovial sarcomas are specifically sensitive to ifosfamide, undifferentiated liposarcomas are the most chemosensitive, leiomyosarcomas are particularly sensitive to the combination of gemcitabine and docetaxel, and angiosarcomas are particularly sensitive to weekly paclitaxel.

After failure to treatment including doxorubicin and ifosfamide in monotherapy or in combination, trabectedine only has Marketing Authorisation for liposarcomas or leiomyosarcomas.

VOTRIENT is an alternative treatment for the management of patients suffering from metastatic soft tissue sarcoma, excluding liposarcoma and GIST, when treatment with anthracyclines or ifosfamide has failed.

# 09 TRANSPARENCY COMMITTEE CONCLUSIONS

**In view of all of the above information, and following the debate and vote, the Committee's opinion is as follows:**

## 09.1 Actual benefit

- Soft tissue sarcomas are serious life-threatening diseases;
- These proprietary medicinal products are intended as specific curative treatments for cancer;
- The efficacy/adverse effects ratio is high;
- There are few medical alternatives to this at this stage of the disease;
- This is a second-line treatment and beyond after failure of chemotherapy with anthracyclines or ifosfamide;

- Public Health Benefit:

  Advanced stage soft tissue sarcomas which have failed on chemotherapy are severe life-threatening diseases which significantly reduce patients' quality of life, but represent a low public health burden because of their rarity.

  Improving the management of these diseases is a public health need included in the established priorities (Second National Rare Diseases Plan, 2011-2014, Second Cancer Plan 2009-2013).

  In light of the progression-free survival data presented (an absolute gain of 3 months) VOTRIENT is expected to have a low impact on the morbidity of patients treated. No improvement on overall survival or quality of life was found in the pivotal study. However, the quality of life data are difficult to interpret as they were only evaluated in the short term (12 weeks) and the EORTC QLQ-C30 questionnaire had not been validated in this disease.

  The transferability of the results of the clinical studies to clinical practice is acceptable (large number of French patients (20%) and the population included was representative of patients seen in medical practice).

  A low positive impact is expected on the organisation of care because of the possible replacement of intravenous chemotherapy with oral VOTRIENT therapy.

  The proprietary medicinal product VOTRIENT should therefore provide a partial response to the identified public health need.

  As a result, this proprietary medicinal product is expected to have a public health benefit in this indication. This benefit is low.

**Taking into account those elements, the Committee evaluates that the actual benefit of VOTRIENT is substantial in the treatment of adult patients with specific subtypes of advanced soft tissue sarcomas (STS) (excluding liposarcoma and GIST), who have previously been treated for metastatic disease with chemotherapy and who have progressed in the 12 months following (neo) adjuvant chemotherapy.**

## 09.2 Improvement in actual benefit (IAB)

VOTRIENT provides a minor improvement in actual benefit (level IV) in terms of efficacy compared with the current treatment strategy.

## 09.3 Target population

Sarcomas are rare tumours with an incidence of approximately 6 new cases per 100,000 people annually representing approximately 4,000 estimated new cases annually in France.[3]
The following calculation of the target population is based on observations from the EMS study (EMS Report 2012), a prospective study exhaustively recording all cases of sarcoma diagnosed between 2005 and 2007.
This EMS study was conducted in the Rhône-Alpes region which represents more than 10% of the French population. The size of the population and geographical area covered by this study and the fact that the Léon Bérard Centre is one of the three NETSARC coordinating centres are evidence supporting the transferability of these data to the national management of sarcoma.
56.5% of these sarcomas diagnosed annually are soft tissue sarcomas. The following histological subtypes have not been considered:

- liposarcomas, for which lack of efficacy was identified in phase II studies,
- GISTs, for which specific treatments are available which were not evaluated in the phase III study,
- osteosarcomas, which are not soft tissue sarcomas.

Two thousand two hundred and fifty-six (2256) soft tissue sarcomas are therefore diagnosed in France annually (excluding liposarcomas and GISTs).
Of these primary diagnoses, 19% are metastatic at diagnosis (n=429) and 26% of patients diagnosed with local STS (n=1827) will progress to metastatic disease (n=475).
Nine hundred and four (904) cases of metastatic STS (excluding liposarcoma and GISTs) are therefore expected annually.
In first line metastatic treatment:

- 69% of patients receive systemic treatment, i.e. 624 patients, 88.5% of whom receive chemotherapy, i.e. 552 patients. Of these, 57.2% reach second line treatment, i.e. 316 patients.
- 31% of patients do not receive systemic treatment as they have been treated with adjuvant or neo-adjuvant anthracyclines and have relapsed within 12 months following the treatment, making it impossible to start an anthracycline as first-line treatment for metastases. This represents 280 patients

Therefore, considering:

- Patients who do not receive any systemic treatment for first-line metastatic disease, n=280
- Patients who receive systemic second-line treatment, n=316

The target population for VOTRIENT in this indication would be approximately 600 patients annually.

# 010 TRANSPARENCY COMMITTEE RECOMMENDATIONS

**The Committee recommends inclusion of VOTRIENT on the list of medicines refundable by National Health Insurance and/or on the list of medicines approved for hospital use in the indication "for the treatment of adult patients with selective subtypes of advanced soft tissue sarcoma (STS) who have received prior chemotherapy for metastatic disease or who have progressed within 12 months after (neo) adjuvant therapy" and at the dosage of the Marketing Authorisation.**

[3] Verhaeghe JL, Rios M, Leroux A, Sirveaux F, Henrot P, Blum A, Marchal F. Traitement des sarcomes des tissus mous de l'adulte: quelle stratégie pour optimiser le traitement. e-mémoires de l'Académie Nationale de Chirurgie 2011; 10 (1): 048-053.

### ◗ Packaging

These are appropriate for the prescribing conditions according to the indication, dosage and duration of treatment.

### ◗ Proposed reimbursement rate: 100%