ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 14 mg hard capsules
ROMVIMZA 20 mg hard capsules
ROMVIMZA 30 mg hard capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ROMVIMZA 14 mg hard capsules
Each hard capsule contains 14 mg of vimseltinib (as dihydrate).

Excipients with known effect
Each hard capsule contains 121.32 mg of lactose monohydrate and 0.0855 mg of the azo colouring agent sunset yellow FCF (E 110).

ROMVIMZA 20 mg hard capsules
Each hard capsule contains 20 mg of vimseltinib (as dihydrate).

Excipients with known effect
Each hard capsule contains 173.32 mg of lactose monohydrate and 0.0075 mg of the azo colouring agent sunset yellow FCF (E 110) and 0.0023 mg tartrazine (E 102).

ROMVIMZA 30 mg hard capsules
Each hard capsule contains 30 mg of vimseltinib (as dihydrate).

Excipient with known effect
Each hard capsule contains 259.98 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Hard capsule.

ROMVIMZA 14 mg hard capsules
The capsule is an orange opaque cap/white opaque body hard capsule of size 4 (approximate length 14 mm), imprinted with “DCV14” in black ink.

ROMVIMZA 20 mg hard capsules
The capsule is a yellow opaque cap/white opaque body hard capsule of size 2 (approximate length 18 mm), imprinted with “DCV20” in black ink.

ROMVIMZA 30 mg hard capsules
The capsule is a light blue opaque cap/white opaque body hard capsule of size 1 (approximate length 19 mm), imprinted with “DCV30” in black ink.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

ROMVIMZA is indicated for treatment of adult patients with symptomatic tenosynovial giant cell tumour (TGCT) associated with clinically relevant physical function deterioration and in whom surgical options have been exhausted or would induce unacceptable morbidity or disability.

4.2 Posology and method of administration

Therapy should be initiated by a healthcare professional experienced in the diagnosis and treatment of conditions for which ROMVIMZA is indicated.

Posology

Recommended dose
The recommended dose of ROMVIMZA is 30 mg taken twice weekly at least 72 hours apart as long as benefit is observed or until unacceptable toxicity.

If the patient misses a dose of ROMVIMZA by less than 48 hours, the patient should be instructed to take the missed dose as soon as possible and return to the usual dosing schedule. If the patient misses a dose of ROMVIMZA by more than 48 hours, the patient should be instructed not to take the missed dose and return to the usual dosing schedule.

Dose reduction
Dose interruptions or dose reductions may be required based on individual safety and tolerability. If patients are unable to tolerate a 30 mg dose of ROMVIMZA, treatment with ROMVIMZA should be temporarily withheld. When the clinical condition of the patient improves, a reduced dose of ROMVIMZA should be given as described in Table 1.

Table 1: Recommended dose reduction

Dose reduction	Twice weekly dose
First	20 mg
Second	14 mg

ROMVIMZA should be discontinued in patients unable to tolerate a 14 mg dose of vimseltinib.

Special populations

Renal impairment
No dose adjustment is recommended in patients with mild or moderate renal impairment (see section 5.2). No clinical data are available in patients with severe renal impairment. Therefore, ROMVIMZA should not be used in these patients (see section 5.2).

Hepatic impairment
No dose adjustment is recommended in patients with mild hepatic impairment (Child-Pugh A). Dose reductions to 14 mg twice weekly for patients with mild hepatic impairment have not been used and efficacy has not been established. No clinical data are available in patients with moderate and severe hepatic impairment. Therefore, ROMVIMZA should not be used in these patients (see section 5.2).

Elderly (≥ 65 years)
No dose adjustments are necessary in patients aged ≥ 65 years (see sections 4.8, 5.1 and 5.2).

Body weight
Dose reductions to 14 mg twice weekly for patients of ≥ 115 kg body weight have not been used and efficacy has not been established.

Paediatric population
ROMVIMZA should not be used in children from birth to pre-pubertal age because of safety concerns based on preclinical safety data (see section 5.3).

The safety and efficacy of ROMVIMZA in children from post-pubertal to less than 18 years of age have not been established (see section 5.1). No clinical data are available.

Method of administration

ROMVIMZA is to be taken orally, with or without food.

Prescribers should instruct patients to swallow the hard capsules whole and not to open, break or chew them. Patients should not ingest the hard capsules if they are broken, cracked, or otherwise not intact as the potential effects of these alterations have not been evaluated.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
Pregnancy (see sections 4.4 and 4.6).

4.4 Special warnings and precautions for use

Long-term safety

The long-term safety of ROMVIMZA has not been established. ROMVIMZA has a novel mechanism of action by inhibition of the colony stimulating factor 1 receptor (CSF1R). The long-term implications of the resulting macrophage depletion, particularly in organs such as the liver, skin, central nervous system and bone marrow are currently uncertain.

Arterial hypertension

Treatment with ROMVIMZA in clinical studies was frequently associated with an increase in blood pressure.

Increase in creatinine

Treatment with ROMVIMZA in clinical studies was frequently associated with an increase in creatinine. The underlying reason is currently unknown.

Embryo-foetal toxicity

Based on data from animal studies, vimseltinib may cause foetal harm when administered to pregnant women (see sections 4.6 and 5.3). Women should be advised to avoid pregnancy while taking vimseltinib. Pregnant women should be informed of the potential risk to the foetus. Women of childbearing potential must use effective contraception during treatment with vimseltinib and for 30 days after the final dose. Effects of vimseltinib on hormonal contraceptives have not been studied. A barrier method contraception should be added if systemic contraceptives are used.

Pruritus

Pruritus has been reported in patients receiving vimseltinib. In the pooled safety population, pruritus was reported in 27% of patients (see section 4.8). Pruritus has also been reported after single doses of vimseltinib in healthy participants. Dose interruptions or dose reductions may be required based on individual safety and tolerability (see section 4.2).

Serum enzyme elevations

Vimseltinib has been associated with serum enzyme elevations, including aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase and creatine phosphokinase (CPK). Although currently these elevations did not result in any cases of liver injury or rhabdomyolysis in clinical studies, this is not excluded since experience in this rare clinical condition is very limited. Thus, ROMVIMZA treatment should be avoided in patients with pre-existing serum transaminase elevations, total bilirubin or direct bilirubin elevations, or active liver or biliary tract disease.

Patients should be monitored for liver function prior to the start of ROMVIMZA, once a month for the first two months and once every 3 months for the first year of therapy and as clinically indicated thereafter.

Excipients with known effect

Lactose
ROMVIMZA contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Sunset yellow FCF (E 110)
ROMVIMZA 14 mg and 20 mg hard capsules contain sunset yellow FCF (E 110), which may cause allergic reactions.

Tartrazine (E 102)
ROMVIMZA 20 mg hard capsules contain tartrazine (E 102), which may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

Effect of other medicinal products on vimseltinib

P-glycoprotein (P-gp) inhibitors
Concomitant administration of single-dose vimseltinib with 200 mg of itraconazole (a P-gp inhibitor) once daily showed that peak exposure (C_{max}) of vimseltinib was comparable to that when administered alone, total exposure of vimseltinib (AUC_{0-t} and AUC_{0-inf}) was approximately 17% to 22% higher in the presence of itraconazole. Dose adjustment is not required.

Proton pump inhibitors
Concomitant administration of vimseltinib with rabeprazole (a proton pump inhibitor) 20 mg once daily under fasted conditions reduced C_{max} and AUC_{0-t} and AUC_{0-inf} of vimseltinib by approximately 21% to 26%, which is not clinically relevant. Dose adjustment is not required.

Effects of vimseltinib on other medicinal products

Breast cancer resistance protein (BCRP) substrates
Vimseltinib is an inhibitor of BCRP *in vitro*. Concomitant use of vimseltinib with BCRP substrates (e.g. rosuvastatin) may increase the concentrations of BCRP substrates and increase the risk of adverse reactions related to these substrates. Clinical studies with BCRP substrates have not been conducted.

The concomitant use of BCRP substrates should be avoided. Refer to the Summary of Product Characteristics of the BCRP substrate for dose modifications if concomitant use cannot be avoided.

Organic cation transporter 2 (OCT2) substrates
Vimseltinib is an inhibitor of OCT2 *in vitro*. Concomitant use of vimseltinib with OCT2 substrates (e.g. metformin) may increase the concentrations of OCT2 substrates and increase the risk of adverse reactions related to these substrates. Clinical studies with OCT2 substrates have not been conducted.

The concomitant use of OCT2 substrates should be avoided. Refer to the Summary of Product Characteristics of the OCT2 substrate for dose modifications if concomitant use cannot be avoided.

P-gp substrates
Vimseltinib is an inhibitor of P-gp *in vitro*. Concomitant use of vimseltinib with P-gp substrates (e.g. digoxin, dabigatran) may increase the concentrations of P-gp substrates and increase the risk of adverse reactions related to these substrates. Clinical studies with P-gp substrates have not been conducted.

The concomitant use of P-gp substrates should be avoided. Refer to the Summary of Product Characteristics of the P-gp substrate for dose modifications if concomitant use cannot be avoided.

Effects of vimseltinib on other substances

Hormonal contraceptives
It is unknown whether vimseltinib may reduce the effectiveness of systemically acting hormonal contraceptives, and therefore women using systemically acting hormonal contraceptives should add a barrier method.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential / Contraception in females

Women of childbearing potential must use effective contraception during treatment with vimseltinib and for 30 days after the final dose. The pregnancy status of women of childbearing potential must be verified prior to initiating vimseltinib and during treatment.
Effects of vimseltinib on hormonal contraceptive have not been studied. Therefore, a barrier method should be added if hormonal contraceptives are used.

Pregnancy

There are no available data from the use of vimseltinib in pregnant women. Based on findings from animal studies, vimseltinib may cause foetal harm when administered to pregnant women (see sections 4.4 and 5.3). Studies in animals have shown reproductive toxicity (foetal structural abnormalities and cardiac malformations, see section 5.3). Vimseltinib is contraindicated in pregnant women (see section 4.3).

Breast-feeding

It is unknown whether vimseltinib is excreted in human milk. A risk to the breast-fed child cannot be excluded. Women should not breast-feed during treatment with vimseltinib.

Fertility

Based on findings from animal studies, ROMVIMZA may impair fertility in males (see section 5.3).

4.7 Effects on ability to drive and use machines

ROMVIMZA has minor influence on the ability to drive and use machines. Fatigue or blurred vision may occur following administration of ROMVIMZA (see section 4.8).

4.8 Undesirable effects

Summary of the safety profile

The safety of ROMVIMZA is based on pooled data from 184 patients with TGCT who received ROMVIMZA at a dose of 30 mg twice weekly in 2 clinical studies. The MOTION study, a phase 3,

double-blind, multicentre, randomised (2:1), placebo-controlled study, included 122 adult patients who received vimseltinib (n = 83) or placebo (n = 39) in the double-blind period; 35 patients crossed over from placebo and received vimseltinib in the open-label period. The phase 1/2 study DCC-3014-01-001 included a total of 66 patients with TGCT who received vimseltinib at a dose of 30 mg twice weekly.

The median duration of treatment in the pooled safety population was 13 months. The median age of patients who received vimseltinib was 44 years (range from 20 to 78 years) and the population was 60% female and 72% White.

The most frequently observed adverse reactions were increased aspartate aminotransferase (AST) (92%), periorbital oedema (63%), increased cholesterol (53%), rash (51%), increased creatinine (43%), decreased neutrophils (36%), fatigue (30%), face oedema (28%), increased alanine aminotransferase (ALT) (27%), pruritus (27%), peripheral oedema (22%) and hypertension (21%).

Grade 3/4 adverse reactions were hypertension (9%), rash (3%), pruritus (3%), decreased neutrophils (3%), periorbital oedema (2%), fatigue (2%), increased cholesterol (1%), neuropathy (0.5%), face oedema (0.5%), generalised oedema (0.5%), and increased AST (0.5%). Serious adverse reactions were peripheral oedema (0.5%) and increased creatine phosphokinase (CPK) (0.5%).

Permanent discontinuation due to an adverse reaction occurred in 7% of patients. The most frequently observed adverse reactions leading to permanent discontinuation were rash (3%), periorbital oedema (2%), neuropathy (1%) and pruritus (1%).

Dose reductions or interruptions due to an adverse reaction occurred in 59% of patients. The most frequently observed adverse reactions leading to dose reductions or interruptions were rash (21%), periorbital oedema (18%), increased creatine phosphokinase (CPK) (17%), pruritus (10%), face oedema (7%), generalised oedema (7%), fatigue (6%) and peripheral oedema (5%).

Tabulated list of adverse reactions

The adverse reactions are listed below by system organ class and frequency categories, defined as: very common (≥ 1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1 000 to < 1/100), rare (≥ 1/10 000 to < 1/1 000), very rare (< 1/10 000), not known (cannot be estimated from the available data). Within each frequency category, adverse reactions are presented in order of decreasing seriousness.

Table 2: Adverse reactions observed in MOTION and DCC-3014-01-001 studies

System organ class	Frequency category	Adverse reaction
Nervous system disorders	Very common	Neuropathy[1]
Eye disorders	Very common	Periorbital oedema[2], lacrimation increased
	Common	Dry eye, vision blurred
Vascular disorders	Very common	Hypertension
Skin and subcutaneous tissue disorders	Very common	Rash[3], pruritus, dry skin
General disorders and administration site conditions	Very common	Peripheral oedema, fatigue, face oedema, generalised oedema
Investigations[4]	Very common	Blood creatine phosphokinase increased[5], aspartate aminotransferase increased, blood cholesterol increased, blood creatinine increased, neutrophil

System organ class	Frequency category	Adverse reaction
		count decreased, alanine aminotransferase increased, alkaline phosphatase increased

[1] Neuropathy comprises peripheral neuropathy, paraesthesia, hypoaesthesia, peripheral sensory neuropathy.
[2] Periorbital oedema comprises eye oedema, eyelid oedema, swelling of eyelid, periorbital oedema, periorbital swelling.
[3] Rash comprises rash, rash erythematous, rash macular, rash maculo-papular, rash papular, rash pruritic, dermatitis acneiform, erythema.
[4] Terms based on laboratory parameters.
[5] Frequency category for blood creatine phosphokinase increased is based on laboratory data from DCC-3014-01-001 only.

Description of selected adverse reactions

Creatine phosphokinase (CPK)
Consistent with the mechanism of action, increased CPK was reported during the MOTION study in vimseltinib-treated patients. The frequency of increased CPK cannot be determined from the MOTION study because CPK was not assessed at baseline. In the phase 1/2 study conducted in 66 patients receiving vimseltinib 30 mg twice weekly, increased CPK was observed in all patients.

Other special populations

Elderly
No overall differences in safety were observed between patients ≥ 65 years of age and patients < 65 years of age.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

In the event of suspected overdose, treatment consists of observation and general supportive measures instituted as required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Antineoplastic agents, protein kinase inhibitors, ATC code: L01EX29

Mechanism of action

Vimseltinib is a selective small molecule tyrosine kinase inhibitor that targets colony stimulating factor 1 receptor (CSF1R). The CSF1/CSF1R signalling axis has a critical role in the development of TGCT. *In vitro* enzyme and cell-based assays have shown that vimseltinib inhibited CSF1R autophosphorylation and signalling induced by CSF1 ligand binding, as well as cellular function and proliferation of cells expressing CSF1R. Vimseltinib also inhibited CSF1R expressing cells and blocked downstream signalling in preclinical models *in vivo*.

Vimseltinib exerts its anti-tumour effects via depletion of CSF1R-dependent macrophages and inflammatory cells.

A decline in the number of hepatic Kupffer cells due to CSF1R inhibition leads to decreased clearance of serum enzymes, including AST, ALT, and CPK. This results in an increase in the serum levels of these enzymes.

Pharmacodynamic effects

Exposure-response relationship
Positive exposure-response relationships were observed between vimseltinib exposure and all grades of oedema, pruritus, rash, and increases of AST ALT, CPK and creatinine.

Clinical efficacy

MOTION, a phase 3, double-blind, multicentre, randomised (2:1), placebo-controlled study, evaluated the efficacy and safety of vimseltinib in patients with symptomatic TGCT with at least moderate pain or at least moderate stiffness for whom surgical resection may have caused worsening functional limitation or severe morbidity. Eligible patients had a confirmed diagnosis of TGCT with measurable disease per the Response Evaluation Criteria in Solid Tumours (RECIST v1.1) with at least one lesion having a minimum size of 2 cm. Patients were randomised to placebo or vimseltinib 30 mg twice weekly for 24 weeks. At Week 25, patients who completed the double-blind, randomised part of the trial were eligible to advance to an ongoing, open-label extension study in which all patients received vimseltinib.

A total of 123 patients were randomised: 40 patients were randomised to placebo and 83 were randomised to vimseltinib during the double-blind period of the study. The median age was 44 years (range 20 to 78 years with 7% of patients ≥ 65 years old); 59% patients were female; 65% were White.

Efficacy was established based on overall response rate (ORR) assessed by blinded independent radiological review (IRR) per RECIST v1.1 at Week 25. Additional efficacy outcomes measured at Week 25 included ORR per tumour volume score (TVS, defined as the estimated volume of maximally distended synovial cavity or tendon sheath involved, measured in 10% increments), active range of motion of the affected joint and patient reported outcomes. All efficacy endpoints achieved statistical significance in the MOTION study.

Overall response rate (ORR)
Statistically significant improvement in ORR was shown in patients randomised to vimseltinib compared with placebo as measured by RECIST v1.1 and TVS based on assessment by IRR. Results for ORR from the MOTION clinical study are summarised in Table 3.

Other key secondary endpoints

Active range of motion
Active range of motion (ROM) was assessed using a goniometer to determine the mean change from baseline, relative to a reference standard, at Week 25. The active ROM measurements showed a clinically meaningful and statistically significant improvement at Week 25 and are presented in Table 3.

Patient-reported outcomes
Additional efficacy measures assessed at Week 25 included physical function (using Patient-Reported Outcomes Measurement Information System-Physical Function [PROMIS-PF]), worst stiffness (using Worst Stiffness Numeric Rating Scale [NRS]), quality of life (using EuroQol Visual Analogue Scale [EQ-VAS]) and worst pain responder (using Brief Pain Inventory [BPI]). The results from patient-reported outcome measures resulted in clinically meaningful and statistically significant improvements at Week 25 in all efficacy parameters and are presented in Table 3.

Table 3: Efficacy results assessed at Week 25

Efficacy parameter	Vimseltinib N = 83	Placebo N = 40
Primary endpoint		
Overall response rate per RECIST v1.1		
Baseline mean (SD) sum of longest diameters, mm	69.1 (42.6)	64.5 (30.8)
ORR (95% CI)	40% (29%, 51%)	0% (0%, 9%)
Complete response	5%	0%
Partial response	35%	0%
p-value	< 0.0001	
Duration of response median (range), months[1,2]	NR (2.5+, 30.9+)	N/A
Key secondary endpoints		
Overall response rate per tumour volume score[3]		
Baseline mean (SD) tumour volume score	10.4 (14.2)	12.8 (17.7)
ORR (95% CI)	67% (56%, 77%)	0% (0%, 9%)
p-value	< 0.0001	
Duration of response median (range), months[1,2]	NR (2.5+, 33.1+)	N/A
Active ROM[4]		
Baseline mean (SD) active ROM, % points[5]	63.0 (29.4)	62.9 (32.2)
LS Mean change from baseline in active ROM (95% CI)[5]	18.4 (5.6, 31.2)	3.8 (-10.5, 18.0)
Difference in LS Means (95% CI)	14.6 (4.0, 25.3)	
p-value	0.0077	
PROMIS-PF		
Baseline mean (SD) PROMIS-PF[5]	39.0 (6.1)	38.5 (6.0)
LS Mean change from baseline in PROMIS-PF (95% CI)[5]	4.6 (2.7, 6.5)	1.3 (-0.5, 3.0)
Difference in LS Means (95% CI)	3.3 (1.4, 5.2)	
p-value	0.0007	
Worst stiffness NRS		
Baseline mean (SD) worst stiffness NRS[5]	5.1 (2.0)	5.2 (1.8)
LS Mean change from baseline in worst stiffness NRS (95% CI)[5]	-2.1 (-2.5, -1.6)	-0.3 (-0.8, 0.3)
Difference in LS Means (95% CI)	-1.8 (-2.5, -1.1)	
p-value	< 0.0001	
EQ-VAS		
Baseline mean (SD) EQ-VAS[5]	61.4 (19.5)	60.2 (20.6)
LS Mean change from baseline in EQ-VAS (95% CI)[5]	13.5 (8.9, 18.2)	6.1 (0.5, 11.8)
Difference in LS Means (95% CI)	7.4 (1.4, 13.4)	
p-value	0.0155	
BPI-30 response[6]		
Response rate (95% CI)	48.2% (37.1%, 59.4%)	22.5% (10.8%, 38.5%)
Difference in responder rate (95% CI)[7]	26.2% (9.5%, 42.8%)	
p-value	0.0056	

NR = Not reached; N/A = Not applicable; BPI = Brief Pain Inventory; CI = confidence interval; LS = least squares; N = sample size; PROMIS-PF = Patient-Reported Outcomes Measurement Information System-Physical Function; ROM = range of motion; SD = Standard deviation.

[1] The median duration of response (DOR) was estimated using the Kaplan-Meier method. "+" indicates that the patient`s response was ongoing at last assessment as of the data cutoff date. DOR results are based on an additional 18 months of follow-up from the time of ORR analysis.
[2] Data cut-off date: 22 February 2025.
[3] TVS was defined as the estimated volume of maximally distended synovial cavity or tendon sheath involved, measured in 10% increments.
[4] Active ROM was assessed using a goniometer and was normalised to a reference standard.
[5] Mean change from baseline was estimated from the mixed model of repeated measures (MMRM) for each corresponding endpoint. Baseline means presented include all participants and not only the ones with data at baseline and Week 25.
[6] BPI response in worst pain is defined as at least a 30% improvement in the mean BPI worst pain NRS score without a 30% or greater increase in narcotic analgesic use at Week 25.
[7] 95% CI for the difference in response rates based on the stratified Mantel-Haenszel method.

In a descriptive analysis conducted at Week 97 in the open-label phase of the study, 19 of 83 patients randomised to vimseltinib (23%) had a best overall response of CR according to RECIST v1.1, as assessed by blinded IRR, with a median time to CR of 11.5 months.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with ROMVIMZA in all subsets of the paediatric population in the treatment of tenosynovial giant cell tumour (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Absorption

Vimseltinib reaches peak plasma concentrations at a median of 1 hour after oral administration of single 30 mg dose of vimseltinib under fasted conditions. Vimseltinib pharmacokinetic (PK) parameters estimated by population PK (popPK) model and provided as geometric mean (coefficient of variation [%]; CV%), were determined following a single oral dose of 30 mg or at steady state following multiple doses of 30 mg twice weekly in TGCT patients. Vimseltinib C_{max} is 283 ng/mL (36%) or 747 ng/mL (39%) after a 30 mg single dose or at steady state, respectively, $AUC_{0\text{-}inf}$ is 46.9 µg*h/mL (45%) after a single dose and $AUC_{0\text{-}24\,h}$ is 13.4 µg*h/mL (45%) at steady state. Steady state plasma concentrations were similar in patients and healthy volunteers and were achieved after approximately 5 weeks with an accumulation ratio of 2.6.

No clinically significant differences in vimseltinib pharmacokinetics were observed following administration of a high-fat meal, compared to fasted conditions.

Distribution

The geometric mean (CV%) apparent volume of distribution (V_z/F) of vimseltinib is 90 L (16%). Vimseltinib is 96.5% bound to human plasma proteins *in vitro.*

Biotransformation

Vimseltinib has no major circulating metabolite. Primary metabolism occurred by oxidation, *N*-demethylation, and *N*-dealkylation; secondary biotransformation pathways included *N*-demethylation, dehydrogenation and oxidation.

CYPs are not anticipated to play a major role in vimseltinib's metabolism.

Elimination

The geometric mean (geometric CV%) apparent clearance (CL/F) of vimseltinib is 0.5 L/h (23%) with an elimination half-life of approximately 6 days following single-dose administration.

Approximately 43% of the dose was recovered in faeces (9.1% unchanged) and 38% in urine (5.1% unchanged) after a single oral radiolabelled dose.

Dose proportionality

Vimseltinib pharmacokinetics are dose proportional.

Special populations

No clinically relevant differences in the pharmacokinetics of vimseltinib were observed based on age (20 to 91 years), sex, race (Asian, Black or African American, White) and body weight (43 to 150 kg).

Renal impairment
Based on a popPK analysis, no significant differences in the pharmacokinetics of vimseltinib were observed in subjects with mild renal impairment (eGFR ≥ 60 mL/min) compared to subjects with normal renal function. Based on limited data, popPK estimated 8% and 27% higher $C_{max,ss}$ and $C_{avg,ss}$ in patients with moderate renal impairment, respectively, but this increase in exposure is not considered clinically relevant. No clinical data are available in patients with severe renal impairment.

Hepatic impairment
In subjects with mild hepatic impairment (Child-Pugh A), AUC_{inf} was 24% lower and C_{max} was 41.5% lower than in matched healthy participants. This reduction in exposure is not considered clinically relevant. PopPK and Pharmacokinetics/Pharmacodynamics (PKPD) modelling estimated that a dose reduction to 14 mg twice weekly in patients with mild hepatic impairment may result in reduced response. No clinical data are available. The effect of moderate to severe hepatic impairment (Child-Pugh B and C) on vimseltinib pharmacokinetics is unknown.

Body weight
PopPK and PKPD modelling estimated that a dose reduction to 14 mg twice weekly in patients with a body weight of ≥ 115 kg may result in reduced response. No clinical data are available.

In vitro findings related to metabolism

In vitro data in human hepatocytes showed that vimseltinib caused a concentration-dependent reduction of CYP1A2 mRNA expression by > 50%, suggesting a down-regulation phenomenon. The clinical relevance of this finding is currently unknown.

5.3 Preclinical safety data

Carcinogenicity

Vimseltinib was not carcinogenic in an oral 6-month transgenic mouse carcinogenicity study at systemic exposures up to 7.6-times the vimseltinib exposure at the recommended human dose based on AUC.
In a 2-year oral rat carcinogenicity study, 2 out of 60 high dose males were identified as having histomorphologically different sarcomas in the synovium of the femorotibial joint at exposures approximately < 1 and 1.4 times (unbound and total, respectively) the recommended human dose based on AUC. Both were classified as sarcoma, not otherwise specified. The relevance of this finding to humans is unknown but considering all available clinical and nonclinical data the carcinogenic risk after vimseltinib administration is considered low.

Developmental and reproductive toxicity

Vimseltinib toxicity was observed in a fertility and early embryonic development study in female rats at approximately 1.6-times the unbound vimseltinib exposure at the recommended human dose based on AUC. Post-implantation loss and increased uterine weights were observed at approximately 6-times

the unbound vimseltinib exposure at the recommended human dose based on AUC. There were no treatment-related effects on mating, fertility, or pregnancy indices, and estrous cycles at any dose level tested. Male rats had lower epididymal and testes weights at approximately 3.6-times the unbound vimseltinib exposure at the recommended human dose based on AUC and there were no treatment-related effects on mating, fertility, or sperm parameters at any dose tested.

Administration of vimseltinib in rats resulted in foetal abnormalities of the cardiovascular (malformations) and skeletal (variations) systems, as well as additional indications of developmental toxicity, at a maternal exposure approximately 7- and 0.9-times the unbound vimseltinib exposure at the recommended human dose based on AUC.
In the pre- and postnatal developmental toxicity study, maternal mortality, total litter losses, reduced fetal body weights, and lower mean pup survival were observed at approximately 1.7-times the unbound vimseltinib exposure at the recommended human dose based on AUC. Total litter loss was also reported in groups treated at doses corresponding to unbound vimseltinib exposures lower than those at the recommended human dose.

In a 26-week repeat-dose toxicity study, recovery male rats that were administered 2.5 or 5 mg/kg/day had moderate to marked reductions in sperm and marked testicular atrophy (1 of 5 and 2 of 5 animals, respectively) corresponding to approximately 1.8 and 3.6-times the unbound vimseltinib exposure at the recommended human dose based on AUC, respectively. In a 39-week repeat-dose toxicity study, minimal to moderate epididymal mineralisation occurred in male dogs administered ≥ 4 mg/kg/day corresponding to exposures lower than the exposure at the recommended human dose based on AUC.

Repeat-dose toxicity

In repeat-dose toxicity studies of up to 26 weeks in rats, there were findings of swollen head and/or limbs, and abnormal teeth at doses of 1 mg/kg/day (approximately 0.96-times the unbound vimseltinib exposure at the recommended human dose based on AUC). The dental effects at doses of 5 mg/kg/day in male rats were associated with lower food consumption and reduced body weight. Chronic progressive nephropathy occurred in animals receiving ≥ 2.5 mg/kg/day (approximately ≥ 1.8-times the unbound vimseltinib exposure at the recommended human dose based on AUC). Degeneration of blood vessels in multiple tissues and increased physis thickness was observed in rats receiving 5 mg/kg/day (approximately 4-times the unbound vimseltinib exposure at the recommended human dose based on AUC).
Low recovery of total radioactivity in mass balance studies and slow elimination of vimseltinib are indicative of potential tissue accumulation. In a rat distribution study, prolonged retention of vimseltinib in eye uveal tract, eye(s), eye vitreous humor, and meninges due to melanin binding was observed. No CNS effects were noted in dogs up to the highest tested dose of 8 mg/kg corresponding to exposure below the anticipated clinical exposure at the recommended human dose. Therefore, clinical relevance of potential accumulation of vimseltinib in meninges remains unknown. Periocular swelling and epiphora observed in dogs at 8 mg/kg at exposures below the expected exposure in humans may be related to prolonged retention of vimseltinib in ocular tissues.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content
Lactose monohydrate
Crospovidone (E 1202)
Magnesium stearate (E 470b)

Capsule shell
Gelatin
Titanium dioxide (E 171)
Brilliant blue FCF (E 133) – 30 mg hard capsule

Erythrosine (E 127) – 30 mg hard capsule
Sunset yellow FCF (E 110) – 14 mg and 20 mg hard capsule
Tartrazine (E 102) – 20 mg hard capsule

Printing ink
Shellac (E 904)
Propylene glycol (E 1520)
Potassium hydroxide (E 525)
Black iron oxide (E 172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.
Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

oPA/Aluminium foil/PVC-film blister with push-through aluminium foil lidding sealed into a child-resistant cardboard wallet pack containing 8 hard capsules.
One carton contains one wallet.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building 4th Floor
Strawinskylaan 3051
1077 ZX, Amsterdam
Netherlands

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1968/001
EU/1/25/1968/002
EU/1/25/1968/003

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation:

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency https://www.ema.europa.eu.

ANNEX II

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building 4th Floor
Strawinskylaan 3051
1077 ZX, Amsterdam
Netherlands

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports (PSURs)**

The requirements for submission of PSURs for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk management plan (RMP)**

The marketing authorisation holder (MAH) shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

Patient card
The MAH shall ensure that a patient card is included in each ROMVIMZA package to address the important potential risk of embryo-foetal toxicity.

- Warning not to take ROMVIMZA if pregnant
- Instruction to use effective contraception methods for women of childbearing potential
- Instruction regarding pregnancy testing before and during treatment
- Information on the importance of reporting pregnancies to healthcare provider

Healthcare professional guide
The MAH shall ensure that, at the time of launch, a healthcare professional guide is distributed to prescribers who are expected to prescribe ROMVIMZA to address the important potential risk of embryo-foetal toxicity.

- Details of the potential risk to the foetus and the importance of informing patients to avoid pregnancy while taking vimseltinib
- Instruction that the pregnancy status of females of childbearing potential must be verified prior to initiating vimseltinib and during treatment
- Instruction that women of childbearing potential must use effective contraception during treatment with vimseltinib and for 30 days after the final dose
- Recommendation for patients to add a barrier method if systemic contraceptives are used as the effects of vimseltinib on hormonal contraceptives have not been studied
- Information on the importance of reporting pregnancies with details of how to report
- Instruction to discontinue vimseltinib immediately if a pregnancy occurs in a female patient during treatment with vimseltinib or within 30 days after the final dose. The patient should be counselled adequately by the HCP and/or referred to a specialist in teratogenicity.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 14 mg hard capsules
vimseltinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 14 mg vimseltinib (as dihydrate).

3. LIST OF EXCIPIENTS

Contains lactose and the azo colouring agent sunset yellow FCF (E 110). See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard capsules

8 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Do not open, break, or chew the capsules.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building 4th Floor
Strawinskylaan 3051
1077 ZX, Amsterdam
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1968/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Romvimza 14 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER – HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

WALLET

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 14 mg hard capsules
vimseltinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 14 mg vimseltinib (as dihydrate).

3. LIST OF EXCIPIENTS

Contains lactose and the azo colouring agent sunset yellow FCF (E 110). See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard capsules

8 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Do not open, break, or chew the capsules.
Read the package leaflet before use.

LIFT HERE

Take this medicine on the **SAME DAYS EACH WEEK**.
Do not take daily.

1. PRESS & HOLD HERE
2. PULL OUT HERE

Opening Instructions
Step 1: Press & hold button gently
Step 2: While holding the button down, pull out the medication card

INSTRUCTIONS:

Dose 1 is the day of the week you begin your medicine. Write the day of the week you begin your medicine on the line below.

Day of the week you begin the medicine.

Based on **Dose 1**, refer to the chart below to determine the day you will take **Dose 2**. (Circle one box).

CIRCLE ONE BOX

DOSE 1: Mon. – Tue. – Wed. – Thu. – Fri. – Sat. – Sun.
DOSE 2: Fri. – Sat. – Sun. – Mon. – Tue. – Wed. – Thu.

The box you circled are the days of the week you will always take your medicine.

WEEK 1 – DOSE 1 – DOSE 2
WEEK 2 – DOSE 1 – DOSE 2
WEEK 3 – DOSE 1 – DOSE 2
WEEK 4 – DOSE 1 – DOSE 2

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building 4th Floor
Strawinskylaan 3051
1077 ZX, Amsterdam
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1968/001

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR WALLET

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 14 mg hard capsules
vimseltinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Deciphera

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 20 mg hard capsules
vimseltinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 20 mg vimseltinib (as dihydrate).

3. LIST OF EXCIPIENTS

Contains lactose and the azo colouring agents sunset yellow FCF (E 110) and tartrazine (E 102).
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard capsules

8 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Do not open, break, or chew the capsules.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building 4th Floor
Strawinskylaan 3051
1077 ZX, Amsterdam
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1968/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Romvimza 20 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

WALLET

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 20 mg hard capsules
vimseltinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 20 mg vimseltinib (as dihydrate).

3. LIST OF EXCIPIENTS

Contains lactose and the azo colouring agents sunset yellow FCF (E 110) and tartrazine (E 102).
See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard capsules

8 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Do not open, break, or chew the capsules.
Read the package leaflet before use.

LIFT HERE

Take this medicine on the **SAME DAYS EACH WEEK**.
Do not take daily.

1. PRESS & HOLD HERE
2. PULL OUT HERE

Opening Instructions
Step 1: Press & hold button gently
Step 2: While holding the button down, pull out the medication card

INSTRUCTIONS:

Dose 1 is the day of the week you begin your medicine. Write the day of the week you begin your medicine on the line below.

Day of the week you begin the medicine.

Based on **Dose 1**, refer to the chart below to determine the day you will take **Dose 2**. (Circle one box).

CIRCLE ONE BOX

DOSE 1: Mon. – Tue. – Wed. – Thu. – Fri. – Sat. – Sun.
DOSE 2: Fri. – Sat. – Sun. – Mon. – Tue. – Wed. – Thu.

The box you circled are the days of the week you will always take your medicine.

WEEK 1 – DOSE 1 – DOSE 2
WEEK 2 – DOSE 1 – DOSE 2
WEEK 3 – DOSE 1 – DOSE 2
WEEK 4 – DOSE 1 – DOSE 2

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building 4th Floor
Strawinskylaan 3051
1077 ZX, Amsterdam
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1968/002

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR WALLET

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 20 mg hard capsules
vimseltinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Deciphera

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 30 mg hard capsules
vimseltinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 30 mg vimseltinib (as dihydrate).

3. LIST OF EXCIPIENTS

Contains lactose. See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard capsules

8 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Do not open, break, or chew the capsules.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building 4th Floor
Strawinskylaan 3051
1077 ZX, Amsterdam
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1968/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Romvimza 30 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC
SN
NN

PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING

WALLET

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 30 mg hard capsules
vimseltinib

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each hard capsule contains 30 mg vimseltinib (as dihydrate).

3. LIST OF EXCIPIENTS

Contains lactose. See package leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

Hard capsules

8 hard capsules

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Do not open, break, or chew the capsules.
Read the package leaflet before use.

LIFT HERE

Take this medicine on the **SAME DAYS EACH WEEK**.
Do not take daily.

1. PRESS & HOLD HERE
2. PULL OUT HERE

Opening Instructions
Step 1: Press & hold button gently
Step 2: While holding the button down, pull out the medication card

INSTRUCTIONS:

Dose 1 is the day of the week you begin your medicine. Write the day of the week you begin your medicine on the line below.

Day of the week you begin the medicine.

Based on **Dose 1**, refer to the chart below to determine the day you will take **Dose 2**. (Circle one box).

CIRCLE ONE BOX

DOSE 1: Mon. – Tue. – Wed. – Thu. – Fri. – Sat. – Sun.
DOSE 2: Fri. – Sat. – Sun. – Mon. – Tue. – Wed. – Thu.

The box you circled are the days of the week you will always take your medicine.

WEEK 1 – DOSE 1 – DOSE 2
WEEK 2 – DOSE 1 – DOSE 2
WEEK 3 – DOSE 1 – DOSE 2
WEEK 4 – DOSE 1 – DOSE 2

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building 4th Floor
Strawinskylaan 3051
1077 ZX, Amsterdam
Netherlands

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/25/1968/003

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTER FOR WALLET

1. NAME OF THE MEDICINAL PRODUCT

ROMVIMZA 30 mg hard capsules
vimseltinib

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Deciphera

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. OTHER

Patient Card
ROMVIMZA
(vimseltinib)

This card contains important safety information that you need to be aware of before taking ROMVIMZA and during treatment with ROMVIMZA. If you do not understand this information, please ask your doctor to explain it to you.

Pregnancy

- Do not take ROMVIMZA if you are pregnant. ROMVIMZA may cause harm to your unborn baby.
- If you are a woman that can become pregnant, you must use effective contraception during treatment with ROMVIMZA and for 30 days after the final dose.
- Before you start ROMVIMZA, talk to your doctor if you are pregnant or plan to become pregnant.
- If you are able to become pregnant, you will need to take a pregnancy test before starting ROMVIMZA and during treatment.
- Contact your doctor immediately if you miss a period, become pregnant, or think you may be pregnant.
- If you become pregnant or plan to become pregnant, ROMVIMZA must be discontinued.

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

ROMVIMZA 14 mg hard capsules
ROMVIMZA 20 mg hard capsules
ROMVIMZA 30 mg hard capsules

vimseltinib

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What ROMVIMZA is and what it is used for

ROMVIMZA contains the active substance vimseltinib, a kinase inhibitor.
It is used in adults to treat tenosynovial giant cell tumours (TGCTs) when it causes problems with physical function and when surgery may result in severe complications or disabilities.

TGCTs are rare tumours that affect the joints. Although these tumours are typically not cancerous, they are locally aggressive and can sometimes grow and cause damage to the joints and tissues around them. In very rare cases, TGCTs can change into cancerous (malignant) tumours.

The active substance in ROMVIMZA, vimseltinib, works by blocking the activity of certain proteins that are involved in the growth of TGCTs.

2. What you need to know before you take ROMVIMZA

Do not take ROMVIMZA if you are:
- allergic to vimseltinib or any of the other ingredients of this medicine (listed in section 6);
- pregnant (see section ‘Pregnancy and contraception’ for more information).

Warnings and precautions

Long-term safety
ROMVIMZA is a new medicine, and the long-term effects are still being studied. It may affect the liver, skin, brain, and other parts of the body.

Some side effects that have been reported include changes in blood tests, skin reactions and increase in blood pressure. There may also be a risk of memory problems, but there are uncertainties about this risk in the long-term.

Talk to your doctor, pharmacist or nurse before taking ROMVIMZA if:
- you have high blood pressure. Treatment with ROMVIMZA may increase blood pressure.
- you are, or plan to become, pregnant. The medicine may cause harm to your unborn baby. Women that can become pregnant must use effective birth control (contraception) during treatment with ROMVIMZA and for 30 days after the final dose. See 'Pregnancy and contraception' for more information.
- your kidneys or liver are not working properly. Your doctor will need to decide if this medicine is suitable for you. In clinical studies, treatment with ROMVIMZA often led to higher levels of a substance called creatinine, which may be a sign of kidney problems. However, there is not enough information yet to fully understand how this might affect your health.
- you have severe itching of the skin (pruritus). Your doctor may temporarily stop treatment or give you a lower dose of ROMVIMZA.
- you know you have high enzyme levels in your blood, or elevated bilirubin levels, or have liver or bile duct disease. Your doctor will need to decide if this medicine is suitable for you.

Regular blood tests
Before starting treatment with ROMVIMZA, your doctor will check your liver health through blood tests. These tests will be done once a month for the first two months, then once every three months during the first year of treatment. After that, tests will be done as needed based on your health condition. The blood tests ensure your liver health remains stable throughout your treatment. This monitoring helps detect any early signs of liver issues. Talk to your doctor, pharmacist or nurse if you have any concerns.

Children and adolescents
This medicine must not be given to children or adolescents under 18 years because there is no information about its use in this age group.

Other medicines and ROMVIMZA
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines obtained without a prescription, vitamins and herbal supplements. This is because they may affect the way ROMVIMZA works or cause side effects.

Tell your doctor if you are taking any of the following medicines. Taking these medicines at the same time as ROMVIMZA may increase the concentrations of these medicines in your body, and increase the risk of side effects related to these medicines:
- rosuvastatin (used to lower cholesterol)
- metformin (used to treat type 2 diabetes by controlling blood sugar levels)
- dabigatran (a blood thinner used to treat and prevent blood clots, and prevent stroke in people with atrial fibrillation, a common heart rhythm problem)
- digoxin (used to treat heart rhythm problems and heart failure)

It is best not to take these medicines with ROMVIMZA. However, if your doctor advises that you must take these medicines, talk with your doctor about how best to take them.

Pregnancy and contraception
ROMVIMZA may cause harm to your unborn baby. If you are pregnant, think you may be pregnant or are planning to have a baby ask your doctor for advice before taking this medicine.

Do not take ROMVIMZA if you are pregnant. If you are a woman that can become pregnant, you must use effective contraception during treatment with ROMVIMZA and for 30 days after the final dose. If using hormonal contraception, add a barrier contraception (such as condoms).

If you are a woman that can become pregnant, you will be asked to take a pregnancy test before you start treatment with ROMVIMZA.

Fertility
In animal studies, this medicine has been shown to reduce sperm quality. It is not known whether this effect occurs in humans. Talk to your doctor if you have any concerns about fertility.

Breast-feeding
Do not breast-feed when taking ROMVIMZA. It is not known if this medicine passes into human milk, so there may be a risk to your breast-fed child.

Driving and using machines
ROMVIMZA has minor influence on your ability to drive or use machines. If you experience an extreme sense of tiredness and lack of energy or blurred vision, do not drive, use tools, or operate machines until you are feeling better.

ROMVIMZA 14 mg, 20 mg and 30 mg hard capsules contain lactose monohydrate
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

ROMVIMZA 14 mg hard capsules contain azo colouring agent sunset yellow FCF (E 110)
It may cause allergic reactions.

ROMVIMZA 20 mg hard capsules contain azo colouring agent sunset yellow FCF (E 110) and tartrazine (E 102)
They may cause allergic reactions.

3. How to take ROMVIMZA

Your treatment will be started by a doctor who is experienced in the treatment of conditions for which ROMVIMZA is indicated. Always take this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

The recommended dose is one 30 mg capsule, taken twice a week, at least 72 hours apart.

The capsules can be taken with or without food.
Swallow the capsules whole with a glass of water and do not open, break or chew the capsules. Do not take any capsules that are broken, cracked, or damaged. The effects of taking broken capsules are not known.

<u>Taking a lower dose</u>
- If you get intolerable side effects after a 30 mg dose, your doctor will temporarily stop the medicine. When your doctor is confident that you are better, you will be given a lower dose (20 mg).
- If you are instructed to take 20 mg, you should take one 20 mg capsule twice a week, at least 72 hours apart, with or without food.
- If you cannot tolerate the 20 mg dose, you will be given a 14 mg dose. You should take one 14 mg capsule twice a week, at least 72 hours apart, with or without food.
- If you cannot tolerate the lowest 14 mg dose or if your doctor considers it not adequate for your condition, ROMVIMZA treatment will be stopped completely.

If you take more ROMVIMZA than you should
If you, or someone else accidentally takes too many capsules, seek urgent medical attention and do not forget to take the medicine package and this leaflet with you.

If you forget to take ROMVIMZA
What to do if you forget to take this medicine will depend on when you realise that you missed a dose. If it is:
- less than 48 hours after the time you should have taken the medicine: take the missed dose as soon as you remember, then take the next dose as usual.
- more than 48 hours after the time you should have taken the medicine: skip the missed dose, then take the next dose at the usual time.

Do not take a double dose to make up for a forgotten dose.

If you stop taking ROMVIMZA
Do not stop taking this medicine without talking with your doctor first. It is important that you continue to take ROMVIMZA even if your symptoms improve and until the doctor decides to stop your treatment.

If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects may occur with this medicine:

Very common (may affect more than 1 in 10 people):
- nerve damage (neuropathy), including nerve damage in the arms and legs, causing pain or numbness, burning and tingling; reduced sensation to touch, pain and temperature;
- swelling around the eye(s) (periorbital oedema), including eyelid(s);
- watery eye(s) (increased lacrimation);
- high blood pressure (hypertension);
- rash, including raised and/or flat reddened rash; itchy rash; small, raised, acne-like bumps; reddening of the skin;
- dry skin;
- itchy skin (pruritus);
- tiredness;
- swelling (oedema) of the face;
- swelling of the arms, legs or ankles (peripheral oedema);
- general swelling;
- abnormal blood test results that show high levels of creatine phosphokinase in your blood;
- abnormal blood test results that show high levels of liver enzymes in your blood;
- abnormal blood test results that show high levels of creatinine in your blood;
- abnormal blood test results that show that you have too much of a fatty substance called cholesterol in your blood;
- blood tests that show that you have low levels of white blood cells (neutrophils).

Common (may affect up to 1 in 10 people):
- dry eye;
- blurred vision.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store ROMVIMZA

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special temperature storage conditions. Store in the original package in order to protect from moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What ROMVIMZA contains

ROMVIMZA 14 mg hard capsules
- The active substance is vimseltinib. Each hard capsule contains 14 mg of vimseltinib (as dihydrate).
- The other ingredients are:
  Capsule content: lactose monohydrate, crospovidone (E 1202) and magnesium stearate (E 470b). See section 2 ‘ROMVIMZA hard capsules contain lactose monohydrate’ for ingredients with known effects.
  Capsule shell: gelatin, titanium dioxide (E 171) and sunset yellow FCF (E 110). See section 2 ‘ROMVIMZA 14 mg hard capsules contain azo colouring agent sunset yellow FCF (E 110)’ for ingredients with known effects. Printing ink: shellac (E 904), propylene glycol (E 1520), potassium hydroxide (E 525), black iron oxide (E 172).

ROMVIMZA 20 mg hard capsules
- The active substance is vimseltinib. Each hard capsule contains 20 mg of vimseltinib (as dihydrate).
- The other ingredients are:
  Capsule content: lactose monohydrate, crospovidone (E 1202) and magnesium stearate (E 470b). See section 2 ‘ROMVIMZA hard capsules contain lactose monohydrate’ for ingredients with known effects.
  Capsule shell: gelatin, titanium dioxide (E 171), sunset yellow FCF (E 110) and tartrazine (E 102). See section 2 ‘ROMVIMZA 20 mg hard capsules contain azo colouring agent sunset yellow FCF (E 110) and tartrazine (E 102)’ for ingredients with known effects. Printing ink: shellac (E 904), propylene glycol (E 1520), potassium hydroxide (E 525), black iron oxide (E 172).

ROMVIMZA 30 mg hard capsules
- The active substance is vimseltinib. Each hard capsule contains 30 mg of vimseltinib (as dihydrate).
- The other ingredients are:
  Capsule content: lactose monohydrate, crospovidone (E 1202) and magnesium stearate (E 470b). See section 2 ‘ROMVIMZA hard capsules contain lactose monohydrate’ for ingredients with known effects.
  Capsule shell: gelatin, titanium dioxide (E 171), brilliant blue FCF (E 133) and erythrosine (E 127). Printing ink: shellac (E 904), propylene glycol (E 1520), potassium hydroxide (E 525), black iron oxide (E 172).

What ROMVIMZA looks like and contents of the pack

ROMVIMZA 14 mg hard capsules
The hard capsule has an orange opaque cap and white opaque body. It is approximately 14 mm in length, imprinted with “DCV14” in black ink. The plastic and aluminium blister contains 8 capsules sealed in a cardboard wallet inside a carton, to cover four weeks of treatment.

ROMVIMZA 20 mg hard capsules
The hard capsule has a yellow opaque cap and white opaque body. It is approximately 18 mm in length, imprinted with “DCV20” in black ink. The plastic and aluminium blister contains 8 capsules sealed in a cardboard wallet inside a carton, to cover four weeks of treatment.

ROMVIMZA 30 mg hard capsules
The hard capsule has a light blue opaque cap and white opaque body. It is approximately 19 mm in length, imprinted with “DCV30” in black ink. The plastic and aluminium blister contains 8 capsules sealed in a cardboard wallet inside a carton, to cover four weeks of treatment.

Marketing Authorisation Holder and Manufacturer
Deciphera Pharmaceuticals (Netherlands) B.V.
Atrium Building 4th Floor
Strawinskylaan 3051
1077 ZX, Amsterdam
Netherlands

For any information about this medicine, please contact the Marketing Authorisation Holder.

This leaflet was last revised in

Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site: https://www.ema.europa.eu.