NIHR | Innovation Observatory

HEALTH TECHNOLOGY BRIEFING
AUGUST 2019

Romiplostim for idiopathic thrombocytopenic purpura in adult patients who are refractory to other treatments

NIHRIO ID	24243	**NICE ID**	10050
Developer/Company	Amgen Ltd	**UKPS ID**	Not Available

Licensing and market availability plans	

SUMMARY

Romiplostim is a medicinal product that is being developed for the treatment of adult patients with idiopathic thrombocytopenic purpura (ITP) who are refractory to other treatments. ITP is the condition of having a low platelet count due to unknown cause. It is also known as immune thrombocytopenic purpura. Many people with ITP do not have symptoms, however people with very low platelet count can have symptoms such as pin prick rash, easy bruising, nosebleeds, gum bleeds, black mouth blisters, fatigue, and heavy periods. Most of the currently available treatments have significant side effects with some treatments leaving patients are at increased risk of infections.

Romiplostim stimulates the production of platelets thereby increasing blood platelet counts and reducing the risk of bleeding. Romiplostim mimics the action of a hormone called thrombopoietin that normally stimulates the production of platelets in the bone marrow. Romiplostim is already licensed in the UK for the treatment of chronic ITP, i.e. those with disease duration of more than 12 months, who are refractory to other treatments. If licensed, romiplostim will offer a new treatment option for adult patients with ITP with disease duration of less than 12 months, who are refractory to other treatments.

PROPOSED INDICATION

Adult immune (idiopathic) thrombocytopenic purpura (ITP) patients (aged ⩾ 18 years old) who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).[a]

TECHNOLOGY

DESCRIPTION

Romiplostim (Nplate) is an Fc-peptide fusion protein (peptibody) that signals and activates intracellular transcriptional pathways via the thrombopoietin (TPO) receptor (also known as cMpl) to increase platelet production. The peptibody molecule is comprised of a human immunoglobulin IgG1 Fc domain, with each single-chain subunit covalently linked at the C-terminus to a peptide chain containing 2 TPO receptor-binding domains. Romiplostim has no amino acid sequence homology to endogenous TPO. In pre-clinical and clinical trials no anti-romiplostim antibodies cross reacted with endogenous TPO.[1]

In the EU/UK, romiplostim is licensed for chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients one year of age and older who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).[1] A variation to the existing marketing authorisation for romiplostim will be sought for the treatment of adult patients with ITP who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).[a] Expansion of the indication for romiplostim to include adult patients with ITP for 12 months or less is supported by data from 311 patients who were diagnosed with ITP within 12 months prior to study enrollment.[2]

The proposed treatment regimen is the same as the current approved indication.[a] Romiplostim should be administered once weekly as a subcutaneous injection. The initial dose of romiplostim is 1 µg/kg based on actual body weight. In adults, future dose adjustments are based on changes in platelet counts only. Treatment should remain under the supervision of a physician who is experienced in the treatment of haematological diseases.[1]

INNOVATION AND/OR ADVANTAGES

Most of the treatments available for ITP until fairly recently had significant side effects for many patients. Because of the immune suppression often used to treat ITP, patients are at increased risk of infection.[3] It is believed that patients with ITP need more flexibility in their treatment options and romiplostim has the potential to play a role earlier in the paradigm.[2] Romiplostim's lack of amino acid sequence homology to endogenous TPO mitigates the risk that antibodies produced against romiplostim will cross-react with endogenous TPO. Furthermore, there are currently no known food or drug interactions with romiplostim as no interaction studies have been performed [1,4]

The submission of a Supplemental Biologics License Application to the FDA is supported by nine studies evaluating the safety and efficacy of romiplostim in adults with ITP, including two long-term open-label extension studies.[2] Subgroup analysis by ITP duration of pooled data from nine studies showed that patient incidences for platelet response at ⩾75% of measurements were higher for romiplostim [ITP ⩽1 year: 74% (204/277)] than for placebo/standard of care [ITP ⩽1 year: 18% (6/34)]. Of patients with ⩾9 months on study, 16% with ITP ⩽1 year discontinued romiplostim and maintained platelet counts ⩾50 × 10^9/l for ⩾6 months without ITP treatment (treatment - free remission). This analysis

[a] Information provided by Amgen Ltd

indicated that romiplostim and placebo/standard of care had similar safety profiles and romiplostim increased platelet counts in patients with either ITP ⩽1 year or ITP >1 year, with more treatment - free remission in those with ITP ⩽1 year.[5]

DEVELOPMENT STATUS AND/OR REGULATORY DESIGNATIONS

Romiplostim is licensed in the EU/UK for chronic immune (idiopathic) thrombocytopaenic purpura (ITP) patients one year of age and older who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).[1]

The most common side effects with romiplostim in adults (seen in more than 1 patient in 10) include headache, infections of the nose and throat and allergic (hypersensitivity) reactions such as rash, itching and rapid swelling under the skin.[6]

Romiplostim was granted orphan drug designation by the European Commission in May 2005 for the treatment of ITP. This product was withdrawn from the Community Register of designated orphan medicinal products in February 2019 at the end of the 10-year period of market exclusivity.[7]

Romiplostim is currently in phase III and phase II clinical development for chemotherapy-induced thrombocytopaenia in adults with non-small cell lung cancer and in adult subjects with gastrointestinal or colorectal cancer, myelodysplastic syndrome, and aplastic anaemia.[8]

PATIENT GROUP

DISEASE BACKGROUND

Idiopathic thrombocytopaenic purpura (ITP) is the condition of having a low platelet count (thrombocytopaenia) of no known cause (idiopathic). As most causes appear to be related to antibodies against platelets, it is also known as immune thrombocytopaenic purpura.[9] Platelets make the blood clot and they are needed to help stop bleeding and bruising after an injury. ITP causes the body's immune system to destroy its own platelets which happens mainly in the spleen. ITP in adults is more common in women than in men and it usually needs treatment.[10]

A normal platelet count is between 150 and 400 (x 10^9/l) of blood. This is usually referred to by doctors using the first three numbers such as 150 or 400. A person is unlikely to get bleeding symptoms unless their platelet count is below 20 x 10^9/L or even 10 x 10^9/L.[10] Some people with ITP, especially those with a count over 50 x 10^9/L, may have no symptoms at all, and their ITP is only noticed during a routine blood test. Patients with platelet counts below 50 x 10^9/L are susceptible to a number of bleeding complications, each with varying degrees of severity and mortality risk. Lower platelet count is associated with increased risk of severe bleeding, and the risk of severe bleeding increases after each unique bleeding episode. Patients with platelet counts 30 – 50 x 10^9/L are at risk of excessive bruising with minor trauma. Patients with platelet count less than 30 x 10^9/L are at increased risk of serious or life-threatening bleeding (e.g. intracranial haemorrhage, mucocutaneous bleeding, lower gastrointestinal bleeding, other internal bleeding and menorrhagia). Life-threatening bleeding, however, rarely occurs in patients with platelet counts above 10 x 10^9/L. Age appears to be an independent risk factor for severe and/or fatal bleeding, with older people at higher risk.[11]

Common symptoms of ITP are petechiae (pin prick rash of blood spots), bruising, nosebleeds, gum bleeds, black mouth blisters, fatigue, heavy periods. Rare symptoms are blood in the eyes,

bleeding from the ears, blood in the urine, bleeding from the stomach, bleeding into the brain.[12] The most serious form of bleeding, intracranial haemorrhage, is rare and is most often seen in older patients who have additional comorbidities and in patients who fail to respond to therapy.[3]ITP that arises suddenly is known as acute ITP, if the platelet count remains low after three months it will be called persistent ITP, and if the platelet count has not returned to normal after 12 months it will be called chronic ITP.[12]

In addition to the bleeding symptoms and low platelet counts, ITP patients experience numerous other limitations such as changes in lifestyle, time spent on doctor and hospital visits, cognitive impairment, fatigue, weakness, depression, increased risk of infection due to ITP per se or due to immunosuppressive therapy or splenectomy, side effects of ITP treatments (especially due to steroids such as weight gain and mood swings), increased risk of bleeding from other treatments such as anticoagulation for arrhythmias or coronary heart disease. Patients may also have fear of bleeding or have concern over increased susceptibility to infection as a result of splenectomy.[13,14] Studies have also shown that ITP can have negative impacts on patient's social life as some patients may have limitation of social and leisure activities, embarrassment of body image, reduction in travel time, , and negative impacts on sexual activities.[15]

CLINICAL NEED AND BURDEN OF DISEASE

The UK incidence of adult ITP is estimated to be around 120 per year.[16] In the UK about 3,000 to 4,000 of the population have ITP at any one time, and it is not more common in any particular racial or ethnic group.[12]

In England in 2017- 2018, there were 14,156 finished consultant episodes (FCE) for ITP (ICD-10 code: D69.3), 13,190 hospital admissions, resulting in 10,756 day cases and 8,218 FCE bed days.[17]

The yearly risk of fatal haemorrhage is around 1.6–3.9%. This risk varies with age, at 0.4% per annum in those below the age of 40 years to 13% per annum over patients over 60 years of age.[3]

PATIENT TREATMENT PATHWAY

TREATMENT PATHWAY

Although treatment for ITP is strictly individualised, specific therapy for ITP may not be necessary unless the platelet count is <20x10^9/L, there is extensive bleeding or patients remain at a high risk of bleeding. Another important consideration is that for some patients the morbidity from side effects of therapy may exceed any problems caused by the thrombocytopenia. Clinical management of this condition must therefore take into account patient's age, the severity of the illness, and the anticipated natural history. Current guidelines consider treatment for ITP appropriate for symptomatic patients and for those at significant risk of bleeding.[18]

If the clinical presentation is not that of a life-threatening bleeding, corticosteroids are considered the standard initial treatment. Intravenous immunoglobulins (IVIG) are generally recommended for patients with critical bleeding and for those unresponsive to corticosteroids or for whom corticosteroids are contraindicated.[18]

CURRENT TREATMENT OPTIONS

First-line treatment include:[18]

- Oral prednisolone, 1 to 2 mg/kg per day, given as single or divided doses (Approx two thirds of patients respond with 10-20% showing long term response. Aim to use for 10- 28 days and taper quickly to avoid steroid related complications)

or

- IVIG (human normal immunoglobulin) 1 g/kg per day for two days (Approx two thirds of patients respond but response is quicker, often within 24 hours, and transient, 3-4 weeks)

Second-line treatment options (for patients with persistent or chronic ITP) include:[18]

- Rituximab

or any of the following

- Mycophenolate mofetil
- Danazol
- Dapsone
- Vinca alkaloids
- Cyclosporin A

Treatment of refractory ITP:[18]

- Romiplostim

or

- Eltrombopag

PLACE OF TECHNOLOGY

If licensed, romiplostim will offer a new treatment option for adult immune (idiopathic) thrombocytopenic purpura (ITP) patients (aged ⩾ 18 years old) who are refractory to other treatments (e.g. corticosteroids, immunoglobulins).

CLINICAL TRIAL INFORMATION

Trial	NCT00415532, EudraCT2006-003700-18, **20060131; adults aged 18 yrs and older; romiplostim vs standard of care (SOC); phase III**
Sponsor	Amgen
Status	Published
Source of Information	Trial registry,[19,20] publication[21]
Location	EU (incl UK), USA, Canada, and Australia.
Design	Randomised, standard of care (SOC)-controlled, open label, parallel assignment.

Participants	n=234; aged 18 yrs and older; diagnosis of ITP, received at least 1 prior therapy for ITP, platelet count < 50,000 or their platelet count falls to < 50,000 during or after a clinically-indicated taper or discontinuation of current ITP therapy.
Schedule	Participants were randomised to: • Romiplostim administered by subcutaneous injection once weekly at a starting dose of 3 µg/kg, adjusted to a maximum dose of 10 µg/kg to maintain a platelet count between 50 and 200 x 10^9/L for up to 52 wks Or • Medical SOC treatments were selected and prescribed by the investigator according to standard institutional practices or therapeutic guidelines and administered for up to 52 wks
Follow-up	Active treatment period: up to 52 wks Follow-up period: 52 wks
Primary Outcomes	Time frame: 52 wks • Number of participants with splenectomy during 52-wk treatment period • Number of participants with treatment failure during 52-wk treatment period
Secondary Outcomes	• Time to splenectomy [Time frame: 52 wks] • Percentage of participants with platelet response [Time frame: wks 1-8, and wks 12, 16, 20, 24, 28, 32, 36, 40, 44, 48 and 52] • Change in ITP-PAQ physical health domain of symptoms [Time frame: baseline and 52 wks] • Change in ITP-PAQ physical health domain of fatigue [Time frame: baseline and 52 wks] • Change in ITP-PAQ physical health domain of bother [Time frame: baseline and 52 wks] • Change in ITP-PAQ physical health domain of activity [Time frame: baseline and 52 wks]
Key Results	The rate of a platelet response in the romiplostim group was 2.3 times that in the SOC group (95% confidence interval [CI], 2.0 to 2.6; P<0.001). Patients receiving romiplostim had a significantly lower incidence of treatment failure (18 of 157 pts [11%]) than those receiving the SOC (23 of 77 patients [30%], P<0.001) (odds ratio with romiplostim, 0.31; 95% CI, 0.15 to 0.61). Splenectomy also was performed less frequently in pts receiving romiplostim (14 of 157 pts [9%]) than in those receiving the SOC (28 of 77 pts [36%], P<0.001) (odds ratio, 0.17; 95% CI, 0.08 to 0.35). The romiplostim group had a lower rate of bleeding events, fewer blood transfusions, and greater improvements in the quality of life than the SOC group.
Adverse effects (AEs)	Serious AEs occurred in 23% of pts (35 of 154) receiving romiplostim and in 37% of pts (28 of 75) receiving SOC, with treatment-related serious AEs being reported in only 5% of pts (7 of 154) and 8% of pts (6 of 75), respectively. Thrombocytopaenia was most common, occurring in 3% of pts (5 of 154) receiving romiplostim and in 12% of pts (9 of 75) receiving the SOC.
Expected reporting date	-

Trial	**NCT00508820, EudraCT2007-000638-37, 20040209; adults aged 18 yrs and older; romiplostim; phase III**
Sponsor	Amgen

Status	Published
Source of Information	Trial registry,[22,23] publication[24]
Location	EU (incl UK), USA, Canada, and Australia.
Design	Single group assignment,open label
Participants	n=407; aged 18 yrs and older; diagnosis of ITP, received at least 1 prior therapy for ITP, platelet count is ≤ 30,000 or the subject is experiencing bleeding that is uncontrolled with conventional therapies.
Schedule	Romiplostim was administered subcutaneously once weekly. Romiplostim was presented as a lyophilized, white powder in 5.0 mL glass vials.
Follow-up	Active treatment duration: up to 4 yrs Follow up: approximately 205 wks
Primary Outcomes	Adverse events [Time frame: duration of treatment plus 30 days or end of study (whichever is later). approximately 205 wks]
Secondary Outcomes	Time frame: duration of treatment [up to 201 weeks] • Platelet response using definition 1 (a doubling of baseline platelet count and a platelet count of >=50 x 10^9/L) • Platelet response using definition 2 (a platelet count increase of >=20 x 109/L from baseline)
Key Results	No new class of adverse events was reported. Platelet responses were achieved by >90% of the patients, typically within 1-2 wks of the initiation of romiplostim treatment. From wk 8, median platelet counts were >100 × 109/l; 47% of the patients received rescue medications (the use decreased over time). This study confirms and extends the tolerability/efficacy findings of previous romiplostim clinical studies.
Adverse effects (AEs)	The rates of treatment-related, serious AEs, serious haemorrhage events, thromboembolic events and fatal events were similar to those reported in previous romiplostim trials (0.2, 0.4, 0.2 and 0.1/100 patient-wks, respectively). Bone marrow reticulin was observed in 4 pts, but biopsies were not routinely performed so the true incidence of this event cannot be determined. Type I collagen (nonserious, unrelated) was reported in 1 pt who likely had myelodysplastic syndrome.
Expected reporting date	-

Trial	**NCT00102336, EudraCT2004-000173-65, 20030212; adults 18 yrs and older; romiplostim vs placebo; phase III**
Sponsor	Amgen
Status	Completed
Source of Information	Trial registry,[25,26] Clinical Study Report[27]
Location	UK, Spain, and USA
Design	Randomised, placebo-controlled, parallel assignment
Participants	n=62; aged 18 yrs and older; diagnosis of ITP; have completed as least 1 prior treatment for ITP (e.g., prednisone); the platelet count must be less than 30 x 10^9/L for those subjects not receiving any ITP therapy, with no count greater than 35 x 10^9/L and less than 50 x 10^9/L for those subjects receiving a constant dose schedule of corticosteroids, azathioprine or danazol with no count greater than 55 x 10^9/L; serum creatinine

	concentration less than or equal to 2 mg/dl (less than or equal to 176.8 µmol/L); adequate liver function, as evidenced by a serum bilirubin less than or equal to 1.5 times the laboratory normal range; haemoglobin greater than 11.0 g/dL.
Schedule	Participants were randomised to: • Romiplostim weekly subcutaneous dosing based on screening weight and platelet count. Starting dose is at 1mcg/kg up to a maximum dose of 15mcg/kg. Romiplostim was supplied in a 5 mL single use glass vial as a sterile, white, preservative-free, lyophilized powder. Or • Placebo weekly subcutaneous dosing based on screening weight and platelet count. Starting dose is at 1mcg/kg up to a maximum dose of 15mcg/kg. Placebo is supplied as a lyophilized power in a 5 mL single use glass vial.
Follow-up	Active treatment duration: 24 wks Follow-up duration: participation was complete once platelet counts were ≤50 $x10^9$/L or the subject reached week 36 with a platelet count > 50 $x10^9$/L, whichever occurred first.[b]
Primary Outcomes	To evaluate the efficacy of romiplostim in the treatment of thrombocytopaenia in subjects with ITP as measured by durable platelet response during the last 8 wks of treatment and other platelet response parameters [Time frame: last 8 wks of treatments]
Secondary Outcomes	• To evaluate the overall safety of romiplostim [Time frame: entire duration of the study including the follow up period] • To evaluate possible reductions in the dose of concurrent ITP therapies while receiving romiplostim [Time frame: entire duration of the study] • To evaluate changes in Patient Reported Outcomes (PRO) and Health Resource Utilization (HRU) due to treatment with romiplostim [Time frame: entire duration of the study]
Key Results	Romiplostim was statistically significantly superior to placebo for the primary efficacy endpoint and for the key secondary endpoints. One subject (4.8%) in the placebo group and 25 subjects (61.0%) in the romiplostim group achieved a durable platelet response (p<0.0001). A total of 3 subjects (14.3%) in the placebo group and 36 subjects (87.8%) in the romiplostim group achieved an overall platelet response (p<0.0001). The number of wks with platelet response was also significantly greater for the romiplostim group: mean 1.3 wks, SD 3.5 wks for placebo; mean 15.2 wks, SD 7.5 for romiplostim (p<0.0001). A total of 13 subjects (61.9%) in the placebo group and 7 subjects (17.1%) in the romiplostim group received rescue medication during the treatment period (p = 0.0004). The placebo group had 61 occurrences of rescue medication use (0.13 per subject*weeks [i.e. number of times rescue medication used/sum (total duration of subject's time in treatment period)]), while the romiplostim group had 54 occurrences (0.06 per subject*weeks). A total of 21 (51.2%) subjects were able to achieve a durable platelet response at a stable dose of romiplostim (no subject in the placebo group) (p = 0.0001) ("stable dose" was defined as a dose maintained within ± 1 µg/kg during the last 8 wks of treatment). Ten subjects in the placebo group and 11 subjects in the romiplostim group were receiving concurrent ITP therapies at baseline. At wk-13 timepoint, 1 of the 10 placebo subjects (10.0%) who entered the study on baseline concurrent ITP

[b] Information provided by Amgen Ltd

	treatment had a > 25% reduction in concurrent ITP treatment and an additional 3 placebo subjects (30%) discontinued all concurrent ITP treatment, while 5 of the 11 romiplostim subjects (45.5%) with baseline concurrent ITP medication had a > 25% reduction and an additional 2 romiplostim subjects (18.2%) had discontinued all concurrent ITP therapies. At wk-25 timepoint, 2 placebo subjects (20.0%) had a > 25% reduction in concurrent ITP treatment and an additional 3 placebo subjects (30.0%) discontinued all concurrent ITP therapies, while 4 romiplostim subjects (36.4%) had a > 25% reduction and an additional 4 romiplostim subjects (36.4%) had discontinued all concurrent ITP therapies. Platelet counts increased above their baseline values by ≥ 20 x 10^9/L at any time during the treatment period for 7 subjects (33.3%) in the placebo group and 38 subjects (92.7%) in the romiplostim group (p<0.0001). Platelet counts in the placebo group remained relatively steady throughout the study, while median platelet count in the romiplostim group increased to a maximum of 100 x 10^9/L at week 11, and then remained at an increased level of between 62.5 x 10^9/L and 96 x 10^9/L for the remainder of the 25-wk treatment period.
Adverse effects (AEs)	The percentage of subjects experiencing AEs was similar in the 2 treatment groups: 95% of the placebo group and 100% of the romiplostim group. A similar percentage of subjects in each group also experienced serious AEs (15.0% placebo, 11.9% romiplostim). AEs that were graded severe occurred in similar a percentage of subjects in each group (25.0% placebo, 19.0% romiplostim), as did adverse events that were graded life-threatening (5.0% placebo, 4.8% romiplostim). No subjects in the placebo group and 1 subject in the romiplostim group died; the cause of death was intracranial haemorrhage 2 wks after discontinuation of romiplostim. The 5 most common adverse events in both treatment groups were fatigue (35.0% placebo, 35.7% romiplostim), contusion (35.0% placebo, 31.0% romiplostim), headache (30% placebo, 26.2% romiplostim), epistaxis (15.0% placebo, 26.2% romiplostim), and arthralgia (25.0% placebo, 23.8% romiplostim). AEs that occurred at a ≥ 10% higher incidence in the romiplostim treatment group than placebo were (placebo, romiplostim) dizziness (0%, 16.7%), abdominal pain (0%, 11.9%), shoulder pain (0%, 11.9%), and epistaxis (15.0%, 26.2%). AEs reported by the investigator as related to investigational product occurred in similar proportions of subjects in the placebo group (20.0%) and the romiplostim group (26.2%). The most common treatment-related events for romiplostim were headache (2 [10.0%] placebo, 5 [11.9%] romiplostim), arthralgia (0 placebo, 3 [7.1%] romiplostim), and injection site bruising (1 [5.0%] placebo, 2 [4.8%] romiplostim). One subject (5%) in the placebo group and 2 subjects (4.8%) in the romiplostim group withdrew from treatment and from the study because of an adverse event. One subject in the placebo group discontinued due to metastasis to liver of severe severity (subject 351). One subject in the romiplostim group discontinued due to B-cell lymphoma of life-threatening severity (subject 1958). An additional subject in the romiplostim group discontinued romiplostim treatment due to a cerebrovascular accident 3 days after the last (21st) dose of romiplostim (platelet count was 107 x 109 /L) (subject 6051). This subject was treated with antiplatelet and antihypertensive therapy for cerebrovascular accident and 10 days later had an intracranial haemorrhage, which ultimately led to death (mentioned above).
Expected reporting date	-

Trial	**NCT00116688, EudraCT2004-000172-13, 20030213; pts aged 1 yr and older; romiplostim; phase III extension**
Sponsor	Amgen =
Status	Published
Source of Information	Trial registry,[28,29] publication[30]
Location	EU (incl UK), USA, Canada, and Australia.
Design	Single group assignment, open label.
Participants	n=313; aged 1 yr and older; previously completed a romiplostim ITP study; Platelet count ≤ 50 x 10 ^9/L.
Schedule	Romiplostim weekly subcutaneous dosing based on screening weight and platelet count. Starting dose of 1 µg/kg up to a maximum dose of 10 µg/kg.
Follow-up	Active treatment duration: up to 5 yrs, follow-up duration: up to 285 wks.
Primary Outcomes	Number of participants with adverse events [Time frame: duration of treatment plus 8 wks (up to 285 wks)]
Secondary Outcomes	• Number of participants with a platelet response [Time frame: duration of treatment (up to 277 wks)] • Number of participants with a reduction or discontinuation of concurrent ITP therapies [Time frame: duration of treatment (up to 277 wks)] • Change from baseline in ITP patient assessment questionnaire [Time frame: baseline to wk 48] • Change from baseline in short form 36 (SF-36) [Time frame: baseline to wk 48] • Change from baseline in Euroqol-5D (EQ-5D) index score [Time frame: baseline to wk 48] • Change from baseline in Euroqol-5D (EQ-5D) visual analogue scale (VAS) [Time frame: baseline to wk 48] • Patient global assessment [Time frame: wk 1 and wk 48]
Key Results	Median platelet counts of 50–200 × 109 per litre were maintained with stable doses of romiplostim (mean 5–8 µg/kg; generally self-administered at home) throughout the study. A platelet response was achieved at least once by 95% of patients, with a platelet response maintained by all patients on a median 92% of study visits. There was a low rate of bleeding and infrequent need for rescue treatments. In conclusion, this study demonstrated that romiplostim was safe and well-tolerated over 614 patient-years of exposure in ITP pts, and that efficacy was maintained with stable dosing for up to 5 yrs of continuous treatment.
Adverse effects (AEs)	Treatment–related serious AEs were infrequent and did not increase with longer treatment. No new classes of AEs emerged. Thrombotic events occurred in 6.5% of pts and were not associated with platelet count.
Expected reporting date	-

ESTIMATED COST

Romiplostim is already marketed in the UK. One pre-filled disposable injection of romiplostim 250 microgram powder and solvent for solution for injection costs £482.00 and one vial of romiplostim 125 microgram powder for solution for injection costs £241.00.[31]

RELEVANT GUIDANCE

NICE GUIDANCE

NICE technology appraisal guidance. Romiplostim for the treatment of chronic immune (idiopathic) thrombocytopenic purpura (TA221). April 2011 (Last updated October 2018).

NHS ENGLAND (POLICY/COMMISSIONING) GUIDANCE

No relevant guidance identified.

OTHER GUIDANCE

- Norfolk and Norwich University Hospitals NHS Foundation Trust. Trust Guideline for the Management of: Newly Diagnosed Immune Thrombocytopenia (ITP) in Children. 2018.[32]
- Matzdorff A, et al. Immune Thrombocytopenia-Current Diagnostics and Therapy: Recommendations of a Joint Working Group of DGHO, ÖGHO, SGH, GPOH, and DGTI. 2018.[14]

ADDITIONAL INFORMATION

Company indicated that there are a total of 9 studies that will support the license variation for romiplostim. This includes, in addition to the clinical trials listed in the "CLINICAL TRIAL INFORMATION" section above, the following clinical trials:[c]

- NCT00102323
- NCT00603642
- NCT00907478
- NCT01143038
- NCT00440037

Amgen Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

[c] Information provided by Amgen Ltd

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