Surrey Heartlands Integrated Care System
Area Prescribing Committee (APC)

Integrated Care Partnership - Surrey Downs, Guildford & Waverley, North West Surrey, and East Surrey Places & associated partner organisations.

NICE Technology Appraisals (TA) for local implementation

NICE TA Guidance name and number	Fostamatinib for treating refractory chronic immune thrombocytopenia TA835		
Available at	https://www.nice.org.uk/guidance/ta835		
Date of issue	19 October 2022	**Implementation deadline**	19 January 2023

Medicine details[1]	
Name and brand name	Fostamatinib (Tavlesse®)
Manufacturer	Grifols UK Ltd
Mode of action	Fostamatinib, through its metabolite R406, blocks the activity of the spleen tyrosine kinase (SYK) enzyme, thereby reducing immune-mediated destruction of platelets.
Licensed indication	TAVLESSE is indicated for the treatment of chronic immune thrombocytopenia (ITP) in adult patients who are refractory to other treatments.
Formulation	100mg and 150mg film-coated tablets.
Dosage	Fostamatinib dosing requirements must be individualised based on the patient's platelet counts. The lowest dose of fostamatinib to achieve and maintain a platelet count of at least 50,000/µL should be used. Dose adjustments are based upon the platelet count response and tolerability. The recommended starting dose of fostamatinib is 100 mg twice daily. After initiating fostamatinib, the dose can be increased to 150 mg twice daily after 4 weeks based on platelet count and tolerability. A daily dose of 300 mg daily must not be exceeded. Once daily fostamatinib should be taken in the morning. Discontinuation Treatment with fostamatinib should be discontinued after 12 weeks of fostamatinib therapy if the platelet count does not increase to a level sufficient to avoid clinically important bleeding.

Comparison of NICE TA with Summary of Product Characteristics (SmPC)[2]	Fostamatinib is licensed for treating refractory chronic ITP, but the company has only provided evidence for using fostamatinib *after* a TPO-RA, or when they are not suitable. The recommendations in NICE are narrower than the marketing authorisation.

NICE TA recommendations[2]

Recommendations

1.1 Fostamatinib is recommended as an option for treating refractory chronic immune thrombocytopenia (ITP) in adults, only if:
• they have previously had a thrombopoietin receptor agonist (TPO-RA), or a TPO-RA is unsuitable
• the company provides fostamatinib according to the commercial arrangement.

1.2 This recommendation is not intended to affect treatment with fostamatinib that was started in the NHS before this guidance was published. People having treatment outside this recommendation may continue without change to the funding arrangements in place for them before this guidance was published, until they and their NHS clinician consider it appropriate to stop.

Decision making framework (DMF)

National guidance and priorities

The ICS has a legal obligation to commission this medicine in line with the NICE TA.
- This NICE TA has been assigned an implementation deadline of 90 days.
- The implementation deadline is 19 January 2023.

Clinical effectiveness

Treatment options for refractory chronic ITP include TPO-RAs, which are mostly followed by rituximab or mycophenolate. Fostamatinib is licensed for treating refractory chronic ITP, but the company has only provided evidence for using fostamatinib after a TPO-RA, or when they are not suitable. Fostamatinib would be used at the same point in the treatment pathway as rituximab or mycophenolate.

Clinical evidence shows that fostamatinib is effective compared with placebo. There is no clinical trial evidence directly comparing fostamatinib with rituximab or mycophenolate. An indirect comparison shows that fostamatinib works better than rituximab at increasing the number of platelets in the blood (cells that help the blood to clot).

The cost-effectiveness estimates for fostamatinib compared with rituximab are within what NICE normally considers an acceptable use of NHS resources. So, fostamatinib is recommended.

Patient safety

- The product should be used within its product license.
- Fostamatinib dosing requirements must be individualised based on the patient's platelet counts.
- Treatment should be discontinued after 12 weeks of fostamatinib therapy if the platelet count does not increase to a level sufficient to avoid clinically important bleeding.

Patient factors

- The patient and clinical experts value individualised treatment. Fostamatinib has a novel mechanism of action and a lack of immunosuppression associated with its use. Alternative treatment options that do not suppress the immune system and could be used when TPO-RAs are not suitable would be highly beneficial.
- A new and additional treatment option would be valued by patients. Some people may be concerned about rituximab's immunosuppressive effects so would prefer an alternative treatment. For people at risk of blood clots, TPO-RAs may not be suitable so fostamatinib could be considered instead. Additionally, treatment options are limited for

people who cannot have TPO-RAs.
- This medicine is available under a homecare service so will be delivered directly to the patient.

Environmental impact

No statement on environmental impact was made in the NICE TA.

- This is an oral medicines which has some packaging waste but less than for sub-cutaneous injections.
- Fostamatinib should be discontinued after 12 weeks if the platelet count does not increase to a level sufficient to avoid clinically important bleeding, so this should reduce medicine wastage.

Equality & diversity

No statement on equality and diversity was made in the NICE TA.

- Age – fostamatinib has a marketing authorisation for treatment in adult patients only.

Place in therapy relative to available treatments

The ITP pathway on the Surrey PAD is based on the pathway from St George's Hospital and local consultants have deemed this to be outdated and a review is required.

NICE states:

'Initial treatment for ITP involves high-dose oral corticosteroids or intravenous immunoglobulin G (IVIgG). Later treatments include:
• TPO-RAs (see NICE's technology appraisal guidance on romiplostim and eltrombopag)
• rituximab
• surgical removal of the spleen (splenectomy)
• azathioprine, mycophenolate, cyclosporine, dapsone and danazol.

The clinical experts explained that the choice of treatment after corticosteroids or IVIgG depends on time to relapse, but clinicians are most likely to offer TPO-RAs. No cost-effectiveness analysis was provided to justify this approach and it should be noted that this assumption differs from the current SH pathway.

They noted that clinicians avoid offering splenectomy in the first year after diagnosis and are unlikely to offer it as a second line of treatment. After TPO-RAs, rituximab and mycophenolate are the most common treatments, but azathioprine is offered to people who want to conceive. Cyclosporine is rarely used because of adverse effects, and dapsone is used as a last resort. The committee understood that danazol is no longer available in the UK. For people with platelet counts higher than 30x109 per litre and at low risk of bleeding, clinicians may adopt a 'watch and rescue' approach. A patient expert explained that once his platelet count had stabilised after treatment with IVIgG, he went onto a watch and rescue approach for 15 years. The committee concluded that the treatment pathway after TPO-RAs includes many treatments, most commonly rituximab and mycophenolate.'

Stakeholder views

The paper was sent out for consultation and 3 comments were received.

Cost-effectiveness

The drug cost per Place according to NICE resources *may exceed* £100,000.

A NICE resource impact template is not included. However using current numbers of patients on TPO-RAs per Place, the discounted price and the assumption that all patients currently on a TPO-RA will move to fostamatinib at the maximum dose and remain on treatment, the cost for one year would then breach the £100,000 per Place per year for all the Places except for East Surrey Place.

This is very crude modelling and for illustration only.

Section 1: cost of the technology

a. Annual cost per patient (or complete course if shorter) for both primary and secondary care:

The list prices of fostamatinib are: (excluding VAT; BNF online, accessed August 2022).

Strength	Price	Pack size	Annual cost (12 packs)
100mg	£3,090	60	£37,080
150mg	£4,635	60	£55,620

b. Availability of CAP/PAS price:
Yes.
The company has a commercial arrangement. This makes fostamatinib available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

c. Price relative to comparable medicines:
Fostamatinib will be used after the thrombopoietin receptor agonists (TPO-RAs). The TPO-RAs with a current NICE TA for use in ITP are romiplostim and eltrombopag.

Further details of the TPO-RA are as follows:

TPO-RA details	Licensed indication	NHS indicative price November 2022 BNF	Approximate annual cost*
Romiplostim Nplate® sc injection. Dose: maximum once weekly dose of 10mcg/kg should not be exceeded.	…adult chronic immune (idiopathic) thrombocytopenic purpura (ITP) patients who are refractory to other treatments (e.g. corticosteroids, immunoglobulins)	125 microgram = £241 250 microgram = £482	£241 x 52 w = £12,532 £482 x 52 w = £25,064 The maximum dose for an adult weighing 75kg would be 750mcg a week and the annual cost would be £75,192
Eltrombopag Revolade® Film coated tablets. Dose: no more than 75mg daily	…patients aged 1 year and above with primary immune thrombocytopenia (ITP) lasting 6 months or longer from diagnosis and who are refractory to other treatments (e.g. corticosteroids, immunoglobulins)	28 x 25mg = £770 28 x 50mg = £1,540 28 x 75mg = £2,310	£770 x 12m = £9,240 £1,540 x 12m = £18,480 £2,310 x 12m = £27,720

*This does not include application of the discount patient access scheme by manufacturers.

Fostamatinib (PAS price) is most likely less expensive than eltrombopag depending on dose used and significantly cheaper than romiplostim. Fostamatinib is significantly more expensive than rituximab.

Section 2: NICE resource impact report and template

a. NICE resource impact report
NICE state that 'We do not expect this guidance to have a significant impact on resources;

that is, the resource impact of implementing the recommendations in England will be less than £5 million per year (or approximately £9,000 per 100,000 population, based on a population for England of 56.3 million people).

This is because fostamatinib is a further treatment option for patients who have not had a suitable response to prior therapy including a TPO-RA, or where use of a TPO-RA is not appropriate, and the overall cost of treatment will be similar to the current treatment options.'

b. NICE resource impact template
A resource impact template is not included.

Commentary:
Costings for maximum of £9,000 per 100,000 population:
Although NICE states that a significant impact on resources is not expected, there is still a new cost pressure even though this may be below the £9,000 per 100,000 population threshold for NICE, as this TA represents a new line of treatment.

At a maximum of £9,000 per 100,000 population, this represents:

	East Surrey	Guildford and Waverley	Surrey Downs	North west Surrey	Surrey Heartlands ICB
Population*	193,532	232,784	316,690	388,466	1,131,472
Cost per Place	£17,418	£20,951	£28,502	£34,962	£101,832

*August 2022 population figures from NHS Prescription Services through ePACT.

Current patient numbers:
The current number of patients (8.11.21 – 8.11.22) on TPO-RAs per Place as identified on Blueteq® is:

	East Surrey	Guildford and Waverley	Surrey Downs	North West Surrey	Surrey Heartlands ICB
Eltrombopag	4	9	10	5	28
Romiplostim	0	2	0	3	5
Total	4	11	10	8	33

Assumptions on potential annual costs:

		East Surrey	Guildford and Waverley	Surrey Downs	North West Surrey	Surrey Heartlands ICB
Total patients		4	11	10	8	33
Assumption - 50% move to fostamatinib in the next year and remain on the treatment						
Number		2	6	5	4	17
Annual costs £	100mg	74,160	222,480	185,400	148,320	630,360
	150mg	111,240	333,720	278,100	222,480	945,540
Cost per patient per year at maximum dose, *using PAS price* to show if above or below threshold of £100,00 per Place.						
		Below	Below	Below	Below	Above
Assumption - 100% move to fostamatinib in the next year and remain on the treatment						
Number		4	11	10	8	33
Annual costs £	100mg	148,320	444,960	370,800	296,640	1,260,720
	150mg	222,480	667,440	556,200	444,960	1,891,080

Cost per patient per year at maximum dose, *using PAS price* to show if above or below threshold of £100,00 per Place.					
	Below	Above for both strengths	Above for 150mg	Above for 150mg	Above for 150mg

This is based on the full price (excluding VAT; BNF online, accessed August 2022). The company has a commercial arrangement which gives the NHS a discount.

The size of the discount is commercial in confidence and prices will be discussed at the APC.

This modelling also does not mitigate the cost by taking into consideration the significant cost of eltrombopag and romiplostim, which has been stopped and other treatments that the patients would have moved to.

Offsetting these existing costs, the additional costs per Place are likely to fall below the £100,000 threshold.

Traffic light recommendation to APC

National Tariff excluded high-cost drug:
Yes

PAD definitions, available at: Traffic Light Status (res-systems.net)

Recommended traffic light status and rationale:
RED – in the current list of drugs excluded from national prices and unit price calculations.

Implementation

NICE TA implementation must be within 90 days of publication.

Actions to implement:

a. Primary care
- This is a National Tariff excluded high-cost drug and is commissioned by ICSs for use in secondary care. There should be no prescribing in primary care.
- Primary care prescribers should be aware that their patient is receiving this medicine and ensure that this is recorded in the patient's notes in order to be alert to potential side-effects and interactions with other medicines prescribed in primary care. This will also ensure that GP records, which are accessed by other healthcare providers, are a true and accurate reflection of the patient's medication.

b. Secondary care
- Providers are NHS hospital trusts.
- Trusts to follow internal governance procedures to add to their formulary and initiate homecare.
- The initiation, administration and on-going treatment is managed by secondary care.
- Specialists will be required to notify the high-cost drugs teams of initiation and response to treatment using the Blueteq® system.
- Homecare arrangements will be managed by the trust.

c. ICS
- This technology is commissioned by integrated care systems.
- Arrangements adopted by the ICS of NHS England's Interim Clinical Commissioning Policy: Thrombopoietin receptor agonists as first line therapy for new or relapsed immune thrombocytopenia in adults during the COVID-19 pandemic, has ceased so patient numbers are not expected to increase substantially.

d. PAD and Joint Formulary
- Rituximab, eltrombopag and romiplostim are currently RED on the PAD.
- The ITP pathway is out of date and needs to be revised. Previous attempts to revise the pathway (which is based on the ITP pathway from St George's University Hospitals NHS FT, our tertiary provider) have failed.

Proposed tick box forms

Blueteq® forms have been developed.

Please consider an initiation form for initial 12 weeks, at which point a continuation form is required. This is based on the SmPC which states that 'Treatment with fostamatinib should be discontinued after 12 weeks of fostamatinib therapy if the platelet count does not increase to a level sufficient to avoid clinically important bleeding'.

References:

1 Specification of Product Characteristics. emc. Available at: Search Results - (emc) (medicines.org.uk) Accessed <8.11.22>

2 NICE Technology Appraisal Guidance: Fostamatinib for treating refractory chronic immune thrombocytopenia. Available at: Overview | Fostamatinib for treating refractory chronic immune thrombocytopenia | Guidance | NICE Accessed <8.11.22>

3 NICE Resource Impact Report: Fostamatinib for treating refractory chronic immune thrombocytopenia. Available at: Tools and resources | Fostamatinib for treating refractory chronic immune thrombocytopenia | Guidance | NICE Accessed <8.11.22>

Declaration of interest:

	Name	Role	Date	Declaration of interests (please give details below)
Prepared by	Tejinder Bahra	MRU Lead Pharmacist	8.11.22	None
Supported by				
Reviewed by	Georgina Randall	MRU Technician	16.11.22	

Explanation of declaration of interest:
None.

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