BEDFORDSHIRE AND LUTON JOINT PRESCRIBING COMMITTEE (JPC)

June 2019

Review: June 2021

Bulletin 276: Iron Chelators for the treatment of iron overload in Myelodysplastic Syndrome (MDS)

JPC Recommendations:-

- To support the recommendations contained in the East of England Priorities Advisory Committee (EoEPAC) Guidance Statement on 'Iron chelators for blood transfusion related iron overload in patients with myelodysplastic syndrome' (see overleaf).
- Any funding requests will be considered via the CCG Individual Funding Request process.

This bulletin replaces JPC Bulletin 214.

Bedfordshire CCG

Luton CCG

The East of England
Priorities Advisory Committee
A function of PrescQIPP

GUIDANCE STATEMENT

Iron chelators for blood transfusion related iron overload in patients with myelodysplastic syndrome

PAC recommendations

1. Routine commissioning of iron chelation agents for the management of iron overload in patients with myelodysplastic syndrome (MDS) is not recommended as there is insufficient clinical and cost effectiveness data to support their use, particularly in relation to overall effects on survival in MDS patients.
2. In low risk MDS patients with a very good prognosis (e.g. patients receiving more than 20 units of red cells transfused, serum ferritin >1000 µg/l where continued red blood cell transfusion is predicted) there is a lack of data on patient numbers, outcomes and cost impact, therefore routine funding for this group of patients is also not recommended. Funding for these patients should be considered either via local individual funding request (IFR) processes or via group prior approval following approval of local business case submission to the relevant area prescribing committee.
3. These recommendations will be reviewed on publication of new evidence of clinical and cost effectiveness.

Key points

The myelodysplastic syndromes (also known as MDS or myelodysplasia) are haematological (i.e. blood-related) medical conditions with ineffective production (or dysplasia) of all blood cells with an incidence of approximately four cases per 100,000 populations per year, predominately affecting the elderly.

Many patients with MDS develop refractory anaemia which is often managed with red blood cell transfusions. Each unit of blood contains iron and as the human body has no physiological mechanism to actively excrete excess iron, repeated blood transfusions result in excessive accumulation of iron which is deposited in various tissues in the body particularly the liver, heart and endocrine organs. This may lead to many complications including cardiomyopathy, liver cirrhosis, diabetes mellitus and reduced life expectancy.

The use of erythropoiesis stimulating agents or epoetins for the management of anaemia has been suggested as a possible alternative treatment strategy in low risk patients to avoid the need for multiple blood transfusions.

Iron chelating agents (desferrioxamine, deferiprone, deferasirox) bind and form a complex with trivalent iron (Iron III) which, unlike unbound iron, is then excreted in either the urine or faeces, and are commonly used in patients with iron overload.

The role of iron chelating therapy in the treatment of iron overload in MDS patients is not well defined. Clinical trial data is lacking and several therapeutic questions remain unanswered. Desferrioxamine

and deferasirox are the only iron chelation agents licensed for use in MDS patients. If indicated, desferrioxamine remains the therapy of choice with the longest record of safety and efficacy of all three agents available. Deferasirox is recommended for patients intolerant of desferrioxamine. Deferiprone is not licensed for use in MDS patients and is therefore not recommended.

There is limited evidence from randomised controlled trials to determine the efficacy and safety of deferasirox, and no head to head studies directly comparing deferasirox with desferrioxamine in MDS patients

Retrospective data from several methodologically limited studies suggest that iron chelation therapy (ICT) can improve survival, reduce cardiac and hepatic complications, lead to haematologic improvements and possibly decrease leukaemia transformation, infectious complications and transplant-related mortality in some patients with lower-risk MDS, (IPSS< 3). Further data is required to establish a clear place in therapy, if any, of iron chelation agents in MDS patients.

Evidence to support the use of dual therapy with both desferrioxamine and deferasirox is limited to case studies.

The British Committee for Standards in Haematology (BCSH) (Dec 2013) confirms that iron chelation therapy cannot be routinely recommended for MDS patients with transfusional iron overload. They recommended that consideration may be given to chelation therapy for patients with a very good prognosis, specifically patients receiving more than 20 units of red cells transfused, serum ferritin >1000 µg/l where continued red blood cell transfusion is predicted. It is not possible to assess the cost impact of funding iron chelation for this subgroup of patients as the number of eligible patients is currently unknown.

There is limited cost effectiveness data in relation to the UK use. In January 2017, the Scottish Medicines Consortium (SMC), following a revised submission by the manufacturer, accepted deferasirox for use as an option in low risk myelodysplasia patients (those with an international prognostic scoring system of low or intermediate risk).[46] Cost effectiveness data considered in the review concluded that deferasirox was cheaper than desferrioxamine, when the equipment costs of £27,890 for deferasirox versus £28,847 for desferrioxamine were factored in, with an associated QALY gain of 0.58. The review discussion confirmed that despite this QALY gain, deferasirox should only be used in accordance with the product licence, in patients who had not tolerated or who were unsuitable for desferrioxamine.

Iron chelating therapies are excluded from the national tariff. Commissioning responsibility for iron chelation therapy in MDS patients was transferred from NHS England (NHSE) to CCGs at the end of March 2015. NHSE had no formally agreed policy on the use of iron chelators in MDS patients at that time.

Where iron chelation is clinically indicated, desferrioxamine remains the agent of choice, however deferasirox may be a cost-effective alternative.

Background

The myelodysplastic syndromes (also known as MDS or myelodysplasia) are haematological medical conditions with ineffective production (or “dysplasia”) of all blood cells.[1,2]

In a patient with a myelodysplastic syndrome, the blood stem cells (immature cells) do not become mature red blood cells, white blood cells, or platelets in the bone marrow. These immature blood cells, called blasts, do not function correctly and either die in the bone marrow or soon after they enter the blood. This leaves less room for healthy white blood cells, red blood cells, and platelets to form in the bone marrow.[1,2]

Prognosis is largely based on the marrow blast percentage, number and extent of cytopenias and cytogenic abnormalities, which are grouped according to the International Prognostic Scoring System (IPSS/IPSS-R). Patients are classified as having low risk MDS (IPSS <3) to high risk (IPSS >4.5) MDS.[3]

Anaemia is usually the most common feature with symptoms including pallor, weakness and fatigue. Other symptoms of MDS include, fever and infections (neutropenia) and increased bruising, petechiae, epistaxis, and mucosal bleeding (thrombocytopenia). Splenomegaly and hepatomegaly are common.[3-6] The anaemia of MDS is primarily managed with red cell transfusions; repeated blood transfusions result in excessive accumulation of iron which is deposited in various tissues in the body particularly the liver, heart and endocrine organs and accumulation can lead to cardiomyopathy and or heart failure, liver failure or diabetes mellitus.[3-6]

This briefing summarises the evidence for the use of iron chelators to manage iron overload and prevent the associated complications in patients with MDS and iron overload.

Iron chelators for the management of iron overload due to frequent blood transfusions in MDS patients

There are three iron-chelating agents available in the UK: desferrioxamine (Desferal® and generic Hospira), deferiprone (Ferriprox®) and deferasirox (Exjade®), which bind and form a complex with trivalent iron (Iron III), which unlike unbound iron, is then excreted in either the urine or faeces.[7-9]

The licensed indications vary between each agent.[7,10-12] Please consult individual summaries of product characteristics (SPCs) for complete instructions relating to dosage, administration precautions and potential adverse effects:[10-12]

The use of erythropoiesis stimulating agents or epoetins for the management of anaemia is a possible unlicensed treatment strategy in low risk MDS patients to avoid the need for blood transfusions and consequent clinical complications from iron overload.

Clinical evidence

Iron chelating agents are commonly used in patients with iron overload from frequent blood transfusions given to treat several conditions including chronic kidney disease, cancer, sickle cell anaemia, Fanconi's anaemia, beta (β-thalassaemia), aplastic anaemia, thrombocytopenia and haemophilia. However, their role in MDS patients is not well defined or established; clinical trial data is lacking and several therapeutic questions remain unanswered. There is over 40 years' experience with the use of desferrioxamine in clinical practice and although there is limited evidence for desferrioxamine in randomised controlled trials, due to the length of historical use it remains the mainstay treatment for iron overload in many conditions including for MDS patients. Desferrioxamine is administered by subcutaneous infusion and whilst it is predominantly supplied via homecare, the infusions are time consuming to set up and are often painful, requiring the introduction of a subcutaneous needle on each occasion which can be distressing; poor compliance with therapy is therefore a key factor in treatment failure.[13] Data in thalassaemia patients indicate that only about 50% of UK patients can adhere fully to current iron chelation therapy and that less adherent patients gain on average only ten years of life, compared to fully compliant patients.[14-16] Both clinicians and patients are therefore keen to consider oral alternatives.

Deferasirox is the only oral iron chelation agent, licensed in patients with MDS as a second line choice for patients who have either failed treatment with or not tolerated desferrioxamine. Deferiprone was the first oral iron chelating agent licensed in the UK, but it is not licensed for use in MDS patients.[7,10-12]

There is limited evidence from randomised controlled trials to determine the efficacy of deferasirox specifically in relation to MDS patients, as the European Medicines Evaluation Agency (EMA) agreed that the safety and efficacy of deferasirox could be extrapolated for all disease states from the data in relation to beta thalassaemia as a model disease.[17] A Cochrane review which aimed to evaluate the place in therapy of oral deferasirox in MDS patients, failed to identify any adequate studies which establish if deferasirox was beneficial in patient with MDS.[33]

There has been one pivotal phase III study for the use of deferasirox in relation to iron overload in beta thalassaemia patients. In study 0107, a phase III, randomised, active controlled, open label trial, 586

patients, older than two years with beta thalassaemia and transfusional iron overload, were randomised to receive either oral deferasirox (n=296) or subcutaneous infusions of desferrioxamine (n=290) for one year.[17-20] The initial dose of deferasirox or desferrioxamine was dependent on the liver iron concentration (LIC) at screening. Deferasirox was taken once daily every morning, 30 minutes before breakfast.

Desferrioxamine was administered as a subcutaneous infusion for ≥8 hours on five consecutive days per week. Blinding was not performed as it was proposed that subcutaneous administration of placebo for 48 weeks to patients randomised to deferasirox was unacceptable.[17-20] The initial doses of deferasirox and desferrioxamine were to remain unchanged during the one year study period unless the evaluation of safety and efficacy markers indicated that dose adjustment was necessary. Patients with a baseline LIC of 2-7mg Fe/g dry weight were allowed to continue their previous doses of desferrioxamine, even if doses were higher than specified by the study protocol as it was considered unethical to reduce the dose of well-managed patients to a sub-optimal level for the purpose of a trial.[18] Blood transfusions were regularly administered during the study period according to the patient's requirements; the amount of blood and iron received by each patient was carefully assessed. The main objective of the trial was to demonstrate non-inferiority of deferasirox compared to desferrioxamine regarding its effects on liver iron concentration (LIC) across all groups.

The primary endpoint was the success rate of deferasirox at reducing or maintaining LIC levels as demonstrated by the change from baseline in LIC levels. In most patients (84%), LIC was determined by liver biopsy. In patients with contra-indications to liver biopsy, mainly children, superconducting quantum interference device (SQUID) biosusceptometer analysis was performed. Non-inferiority was demonstrated if the lower limit of the 95% confidence interval for the difference in success rate between deferasirox and desferrioxamine was above -15% in the primary efficacy population.[17-20]

The mean age of the patients was 17 years with a median of 15 years. Many of the patients were under 16 years of age (51%). Approximately two thirds of each group had a baseline LIC value of 7mg Fe/grams dry weight (g.dw) or more at baseline; 69% in the deferasirox group and 68% in the desferrioxamine group. Most patients completed one year of therapy: 541 (92.3%) of 586 underwent both baseline and one year LIC assessments. In the primary efficacy population, non-inferiority of deferasirox to desferrioxamine was not demonstrated. The success rate for deferasirox group (n=146) was 52.9% and for desferrioxamine (n=184) was 66.4%. The difference between the groups was -13.5% (95% CI -21.6, -5.4) i.e. 13.5% in favour of desferrioxamine. The lower limit confidence interval indicates that the response rate to deferasirox could be up to 21% lower than that achieved with desferrioxamine. Therefore, in the primary efficacy population, non-inferiority of deferasirox to desferrioxamine was not demonstrated, but was explained by the study authors as being possibly due to proportionally lower doses of deferasirox relative to desferrioxamine being administered to patients with LIC values <7mg Fe/g.dw. Non-inferiority was demonstrated in the group of patients who were allocated to the higher dose groups.[17-20]

In a subgroup analysis of 381 patients with LIC ≥7mgFe/g.dw who received deferasirox doses above 20mg/kg and desferrioxamine ≥35mg/kg, the difference in success rate between the two groups was -0.35% [-10.2, 9.6] in favour of desferrioxamine. If only patients who had LIC determined by biopsy are included, the success rate for deferasirox (n=176) was 59.7% and with desferrioxamine (n=179) was 58.7% with a difference and 95% CI of 1.0% (-9.2, 11.2). In both these analyses, the lower limit of the CI is above -15%. In patients with baseline LIC values less than 7mg Fe/g.dw, who received either deferasirox at doses of 5mg or 10mg/kg per day (n=34), the success rate was 40%. The success rate in the comparable desferrioxamine group (n=72) was 82.8%. The between group difference was -42.8% (-55.9,-29.7%). A mean reduction in LIC of -5.3 ± 8.0mg Fe/g.dw (p<0.001) occurred in the deferasirox group and of -4.3 ± 5.8mg Fe/g.dw in the comparable desferrioxamine group. The difference between the two groups was not statistically significant (p=0.367).[17-20]

Discontinuations were relatively similar in the groups receiving deferasirox (n=17) and desferrioxamine (n=12).[17-20] Patient satisfaction was assessed at four and 24 weeks, and at the end of the study.

Significantly more patients on deferasirox previously treated with desferrioxamine indicated they would be willing to continue deferasirox, compared with patients on desferrioxamine who would be willing to continue desferrioxamine (85.8% vs.13.8%, p<0.001).

Larger phase 2 studies in several different conditions have shown a clear reduction in serum ferritin and labile plasma iron species over one to two years of therapy with deferasirox, however the studies only included 47 MDS patients out of 1009 total patient population.[21-26]

There is a small amount of limited data, mainly from analysis of case series and retrospective reviews, which suggests that deferasirox is effective in the management of iron overload in MDS patients and is associated with a reduced mortality risk and improvement in liver function in low risk patients.[27-32] More data is required to confirm overall benefit in MDS patients and superiority over desferrioxamine.

Tolerability of oral treatment remains unclear. Only half of all patients complete one year of therapy with either deferasirox of deferiprone, most due to non-treatment related adverse events, however a significant proportion of patients experience unacceptable gastro intestinal side effects.[29,30,33,34] A Cochrane review comparing desferrioxamine and deferiprone, has stated that no major differences in compliance between the two treatments was observed as almost all those in the included trials achieved good to excellent compliance with both treatments.[34]

A small number of case reports have suggested that the use of dual therapy, involving desferrioxamine plus deferasirox, may be effective in certain patients, however more information is required to confirm place in therapy.[35-37]

Guidance produced by the British Committee for Standards in Haematology (BCSH) in 2013 and European Society for Medical Oncology (ESMO) 2014, provides the following recommendations and guidance:[3,38]

- Iron chelation therapy cannot be routinely recommended for MDS patients with transfusional iron overload.
- Consideration may be given to chelation therapy for patients with a very good prognosis, specifically patients with WHO classifications of Refactory Anaemia (RA), Refractory anaemia with ringed sideroblasts (RARS) and Myelodysplastic syndrome associated with isolated del(5q).. Triggers may include more than 20 units of red cells transfused, serum ferritin >1000 µg/l in patients for whom continuing red cell transfusion is predicted.
- Patients treated with iron chelation therapy should ideally receive this treatment within clinical trials.
- Desferrioxamine remains the therapy of choice with the longest record of safety and efficacy in MDS. Deferasirox is recommended for patients intolerant of desferrioxamine. Deferiprone could be considered in patients with normal baseline neutrophil counts.

It is also noted in these guidelines that while heart iron overload is a well-documented cause of heart failure in children with thalassaemia, its incidence and clinical consequences are less certain in MDS patients as many already have other causes of cardiac morbidity. Conversely data from heart MRI studies show that heart iron overload (reflected by a decrease in MRI heart T2*) is frequent in patients having received at least 70-80 RBC concentrates or more, a frequent situation in low-risk MDS, and that a heart T2* value <20ms is associated with decreased ventricular ejection fraction and a risk of heart failure. In the absence of prospective studies, published recommendations for iron chelation therapy so far only result from expert opinions, which generally advocate starting chelation in patients with relatively favourable prognosis (i.e. low or intermediate- 1-risk MDS), who have received 20–60 RBC concentrates, or if serum ferritin raises above 1000–2500 ug/l or if cardiac T2* is significantly reduced.[3,38]

Cost impact and cost effectiveness

Iron chelating therapies are excluded from the national tariff. Commissioning responsibility for iron chelation therapy in MDS patients was transferred from NHS England (NHSE) to CCGs at the end of March 2015. NHS England commission iron chelation therapy for patients with chronic inherited anaemias.[39]

Table 1: Comparative costs of Iron chelation

Drug	Usual dosage	Cost per year
Desferrioxamine	20-60mg/kg daily by subcutaneous infusion for 5-7 days, every week.	£2,770 - £15,524 [£1,746 - £10,465]*
Deferasirox	20-30mg/kg once daily	£12,230 - £18,346

NHS prices from MIMS December 2016. Costs are approximate and are based on an average body weight of 54kg, which has been suggested as the mean patient weight for patients needing iron chelation therapy. Doses are shown for general comparison and do not imply therapeutic equivalence. The cost in brackets* is indicative of the treatment costs if medicines were purchased through an agreed NHS contract, such as via secondary care provider and home care company.

While the drug cost of desferrioxamine is relatively low, additional costs to the NHS may be incurred (e.g. home care delivery or nurse services).[40] The overall costs in relation to the administration of both parenteral desferrioxamine and blood transfusion are complicated and unclear due to the number of variables involved.

In addition, the infuser device used may significantly affect cost effectiveness; (e.g. use of a Graseby pump plus associated equipment will add a further £500-£1,000 for the first year rising to an additional £16,500 per annum should an elastomer balloon delivery system be used). The costs of regular laboratory monitoring of liver and renal function will also need to be considered. These may be higher in patients taking deferasirox.[41,42] Exact prices may vary and be dependent on locally negotiated contracts. Individual Trusts need to confirm local cost comparisons.

The incidence of MDS is approximately four cases per 100,000 population per year.[2,3,43] It is predominately a disease of the elderly with an incidence of >30 cases per 100,000/per year, with a median age of diagnosis of 70. However, patients as young as two years have been reported. It is more common in men and white patients.[2,3] The number of patients requiring iron chelation is estimated as one per 100,000 population.[44] In relation to the management of heart failure (a possible complication of iron overload), non-elective spell costs are currently between £2,288-3,668 per episode, with £208/day, long stay supplement when the spell goes past the trimpoint for the HRG code.[45]

There is limited cost effectiveness data available in relation to the UK use of all iron chelators in MDS patients. A cost utility analysis study conducted by Karnon et al has estimated the resource use and costs for equipment for desferrioxamine treatment to be £7,552 annually per patient.[40] This study was funded by Novartis Pharmaceuticals Limited. The analysis assumed that deferasirox has equivalent efficacy to desferrioxamine and that patients receiving deferasirox are similarly compliant with patients receiving desferrioxamine infusions. Costs relating to monitoring and adverse events were also assumed to be similar. The analysis calculated that deferasirox is expected to gain quality adjusted life years (QALY) at an additional cost of £891 per QALY gained.

In January 2017, the Scottish Medicines Consortium (SMC), following a revised submission by the manufacturer, accepted deferasirox for use as an option in low risk myelodysplasia patients (those with an international prognostic scoring system of low or intermediate risk).[46] Cost effectiveness data considered in the review concluded that deferasirox was cheaper compared to desferrioxamine, when the equipment costs of £27,890 for deferasirox versus £28,847 for desferrioxamine were factored in, with an associated QALY gain of 0.58. The review discussion confirmed that despite this QALY gain,

that deferasirox should only be used in accordance with the product licence, in patients who had not tolerated or who were unsuitable for desferrioxamine infusions. Feedback obtained during this original SMC submission highlighted the small number of MDS patients included in the trial numbers; 47 out of 1009. In patients with beta thalassaemia the cost per QALY was around £20,000, in patients with sickle cell disease it was around £30,000 per QALY and in patients with myelodysplastic syndrome it is over £38,000 per QALY. From this, the SMC concluded that the cost effectiveness of deferasirox was acceptable in patients with beta thalassaemia and sickle cell disease but the case had not been demonstrated in patients with MDS.[42]

Data from other health economies, including the US, suggest that deferasirox may be a cost-effective alternative to traditional desferrioxamine. A study published in the Journal of Medical Economics in 2010 evaluated the cost effectiveness of deferasirox compared to desferrioxamine in the treatment of iron overload in lower-risk, transfusion-dependent MDS patients. The evaluation was based on the results from a cohort of 1000 patients. The incremental cost per QALY gained with deferasirox was £20,822 however this was dependent on the dose of deferasirox used. A dose of 15mg/kg was shown to be less expensive than desferrioxamine whereas a higher dose of 25mg/kg resulted in the incremental cost per QALY gained rising to over $40,000 (approx. £25,000).[47] This paper was evaluated by the Centre for Reviews and Disseminations (CRD), University of York. The CRD concluded that although the authors of the study reported that deferasirox was cost effective, the results were based on assumed clinical efficacy as there was no clinical trial evidence available at the time of the study.[48]

The US economic case for deferasirox over desferrioxamine published in the American Journal of Haematology in May 2011 suggested that the increased costs for oral deferasirox would be offset by the avoidance of costs involved in administration and monitoring of desferrioxamine (i.e. in administration and maintenance of indwelling catheters, infusion devices for subcutaneous administration).[49] Through economic modelling, the article suggested that the use of deferasirox is likely to be more cost-effective than desferrioxamine in MDS patients: estimated to be $31,233 to $57,000 (approximately £24,000 to £44,000 for desferrioxamine versus $19,000 to $35,000 (approximately £14,500 to £270,00) for deferasirox per QALY gained. However, these economic models are yet to be validated prospectively in clinical studies.

A Canadian model, published in 2011, analysed the cost effectiveness of deferasirox compared with no chelation and concluded that treatment with deferasirox would provide added value at an acceptable cost (i.e. $50,000 to $100,00 Canadian dollars; £28,000 to £56,000) per QALY gained for the treatment of lower risk MDS patients.[50]

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Document history

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Appendix 1: Assessment against Ethical and Commissioning Principles

Treatment assessed	Iron chelation for Myelodysplastic Syndromes (MDS)
East of England PAC recommendations	Routine commissioning of iron chelation agents for the management of iron overload in patients with Myelodysplastic syndrome (MDS) patients is not recommended as there is insufficient clinical and cost effectiveness data to support their use, particularly in relation to overall the effects on survival in MDS patients. For existing patients, where there is documented evidence that funding for treatment was approved by NHS England prior to March 2015, ongoing funding should be approved by CCGs and treatment continued until the patient and their NHS clinician consider it is appropriate to stop.

Clinical effectiveness	There is limited evidence for the use of desferrioxamine from randomised controlled trials, however there is over 40 years experience with its use in the management of iron overload, including in MDS patients.There is limited evidence for deferasirox from randomised controlled trials to determine the efficacy and safety specifically in relation to MDS patients, as the European Medicines Evaluation Agency (EMA) agreed that the safety and efficacy of deferasirox could be extrapolated for all disease states from the data in relation to beta thalassaemia as a model disease. There has been one pivotal phase III study for the use of deferasirox in relation to iron overload in beta thalassemia patients. In study 0107, a phase III, randomised, active controlled, open label trial, 586 patients, older than 2-years with beta thalassaemia and transfusional iron overload were randomised to receive either oral deferasirox (n=296) or subcutaneous infusions of desferrioxamine (n=290) for one year. Non-inferiority was not demonstrated in the primary efficacy population. In a subgroup analysis of 381 patients with LIC ≥7mgFe/g dry weight who received deferasirox doses above 20mg/kg and desferrioxamine ≥35mg/kg, the difference in success rate between the two groups was -0.35% [-10.2, 9.6] in favour of desferrioxamine. If only patients who had LIC determined by biopsy are included, the success rate for deferasirox (n=176) was 59.7% and with desferrioxamine (n=179) was 58.7% with a difference and 95% CI of 1.0% (-9.2,11.2). In both these analyses, the lower limit of the CI is above -15%. In patients with baseline LIC values less than 7mg Fe/g dry weight, who received either deferasirox at doses of 5mg or 10mg/kg per day (n=34), the success rate was 40%. The success rate in the comparable desferrioxamine group (n=72) was 82.8%. The between group difference was -42.8% (-55.9,-29.7%) [37]. A mean reduction in LIC of -5.3 ±8.0mg Fe/g dry weight (p<0.001) occurred in the deferasirox group and of-4.3 ± 5.8mg Fe/g dry weight in the comparable desferrioxamine group. The difference between the two groups was not statistically significant (p=0.367). Larger phase 2 studies in several different conditions have shown a clear reduction in serum ferritin and labile plasma iron species over 1–2 years of therapy, however the studies only included 47 MDS patients, out of 1009 total patient population. There is a small amount of limited data, mainly from analysis of case series and retrospective reviews, which suggests that deferasirox is effective in the management of iron overload in MDS patients and is associated with a reduced mortality risk and improvement in liver function in low risk patients. Deferiprone is not licensed for use in MDS patients.

Cost effectiveness	There is limited cost effectiveness data available in relation to the UK use of all iron chelators in MDS patients. Data from small cost utility analyses suggest that oral deferasirox could be a cost-effective alternative to alternative to desferrioxamine. In January 2017, the Scottish Medicines Consortium (SMC), following a revised submission by the manufacturer, accepted deferasirox for use as an option in low risk myelodysplasia patients (those with an international prognostic scoring system of low or intermediate risk). Cost effectiveness data considered in the review concluded that deferasirox was cheaper than desferrioxamine, when the equipment costs of £27,890 for deferasirox versus £28,847 for desferrioxamine were factored in, with an associated QALY gain of 0.58. A previous submission in February 2007 had allowed deferasirox for restricted use within NHS Scotland in for the treatment of chronic iron overload associated with the treatment of rare acquired or inherited anaemias requiring recurrent blood transfusions; but not for patients with myelodysplastic syndromes.
Equity	None identified.
Needs of the community	The needs of the community are low. The number of patients within this cohort is small and has been estimated as 1 per 100,000 population.
Need for healthcare (incorporates patient choice and exceptional need)	The need for iron chelation therapy in this cohort of patients is because of a complication due to the use of blood transfusions in the management of the MDS. There are limited therapeutics alternatives and no treatment could lead to cardiac failure, liver failure, diabetes and may increase mortality risk for the patient.
Policy drivers	The main policy driver is the transfer of funding from NHSE to CCGs in March 2015. At this time, NHS England was funding iron chelation treatment for certain patients. Consequently, there are a cohort of patients already receiving treatment who require funding to be continued.
Disinvestment	None