二零零八年六月二十四日
資料文件

立法會衞生事務委員會
為公立醫院的地中海貧血病患者提供的排鐵療法

目的

本文件旨在向委員闡述公立醫院為地中海貧血病患者提供的排鐵療法。

背景

2. 地中海貧血病是一種影響紅血球的遺傳性血病。紅血球中含有血色素和鐵質，負責輸送人體所需氧氣。地中海貧血病會令人體減少產生健康的紅血球，而不正常的紅血球亦會在人體內加速分解，以致體內紅血球的帶氧量減少。

3. 嚴重地中海貧血病的標準療法是定期為患者輸血，以補充紅血球。患者通常每數星期需要輸血一次。在每次輸血相隔期間，紅血球會在體內緩慢地分解。然而，當紅血球分解後，鐵質仍會留在體內。由於人體無法自然排出多餘的鐵質，因此，接受輸血的地中海貧血病患者，須接受把多餘鐵質排出體外的治療，否則鐵質會積聚在心臟、肝臟和內分泌腺等內臟，最終會導致多器官功能障礙。這種除鐵治療稱為排鐵療法。

4. 醫院管理局(醫管局)現時提供三種排鐵鉗合劑，即去鐵胺 (Desferrioxamine)、去鐵酮 (Deferiprone)及地拉羅司 (Deferasirox)。

去鐵胺 *(Desferrioxamine)*

5. 去鐵胺能將體內的鐵分子鉗緊或黏合，然後經尿液或糞便排走。去鐵胺通常是以打針機慢慢注射入皮下。這種方法

稱為皮下注射。患者每星期需要接受治療五至七次，每次需時八至十二小時。這種排鐵鉗合劑在市場已超過四十年，生產商為 Novartis。

去鐵酮 *(Deferiprone)*

6. 去鐵酮是第二線藥物，用於忌用去鐵胺、對去鐵胺不耐或不適合使用去鐵胺的重型地中海貧血病患者。去鐵酮是口服藥物，須每天服用三次。這種藥物在一九九九年八月推出市場，生產商為 Apotex.

地拉羅司 *(Deferasirox)*

7. 地拉羅司是一種口服的排鐵鉗合劑，須每天服用一次。地拉羅司在醫管局現被列為自費購買藥物。這種藥物於二零零五年十一月推出市場，生產商為 Novartis。

8. 有關這三種藥物的療效、副作用及費用等資料，表列於附件。

醫管局引進藥物

9. 隨着醫療科技迅速發展，藥劑市場每年都有很多新藥面世。對於會否把個別藥物納入醫管局藥物名冊（名冊），這涉及科學實證評估結果、臨牀倫理和複雜臨牀決定，以及專業討論和審議工作。此外，把新治療模式與現行的療法作比較須有確實的醫學背景資料支持。

10. 基於須以公平和有效的方法運用公共資源，以及使醫管局能以有限資源為更多病人提供服務的原則，在決定應否把某種藥物納入醫管局的標準治療程序時，必須考慮其臨牀療效、安全程度、成本效益及機會成本。

11. 大部分由醫管局提供的藥物均獲政府大幅津貼，並獲納入名冊內。但以下三大類藥物並無津貼，須由病人自費購買：

(a) 僅具初步醫療驗證的藥物；
(b) 與其他替代藥物相比僅具邊際效益的藥物；以及
(c) 生活方式的藥物。

12. 當局在考慮以上三種排鐵藥物在名冊內的定位時，是以上文所述的臨牀療效、安全、成本效益、機會成本和促進病人的選擇等原則為指引。去鐵胺及去鐵酮現時均已列入醫管局獲高補貼的標準治療範圍。去鐵胺被列為普通藥物，而口服的去鐵酮則被列為專用藥物。至於地拉羅司，則屬於具初步醫療驗證和邊際效益的藥物，而費用遠較另外兩種藥物為高。此外，就該藥物推出市場後所作的監控結果發現有病人服用後可能出現嚴重副作用及致命併發症的個案。醫管局自二零零七年四月起將此藥物列為自費藥物。

總結

13. 我們明白病人會期望某種藥物可列入名冊內作為標準治療。為此，醫管局一直透過建立已久的聯絡渠道與病人組織保持定期溝通，以了解和回應他們對把新藥物引入名冊等事宜的關注，確保他們的意見獲得充分反映。不過，醫管局把有限的公共資源合理地用於最能切合社會所需的服務，是較為審慎的做法。醫管局會繼續定期檢討名冊，並基於可用的替代藥物、良好的醫療水平、為病人提供有效的治療，以及合理地運用資源的考慮，定期評估新藥物。

徵詢意見

14. 請委員閱悉本文件內容。

食物及衞生局
醫院管理局
二零零八年六月

附件

（只有英文版本）

A summary of the features of Desferrioxamine, Deferiprone and Deferasirox

(Note: The summary is compiled on the basis of the list of references at Appendix.)

	Desferrioxamine (Desferal®)	**Deferiprone (Ferriprox®)**	**Deferasirox (Exjade®)**
Manufacturer	Novartis	Apotex	Novartis
Licensed indication	Treatment for chronic iron overload, e.g. - -transfusional haemosiderosis in patients receiving regular transfusions (e.g. thalassaemia major). - primary and secondary haemochromatosis in patients in whom concomitant disorders (e.g. severe anaemia, cardiac disease, hypoproteinaemia) preclude phlebotomy.	Treatment of iron overload in patients with thalassaemia major when desferrioxamine therapy is contraindicated or inadequate.	Treatment of chronic iron overload due to blood transfusions (transfusional haemosiderosis) in patients 2 years of age and older
Route of administration	slow subcutaneous infusion over 8-12h, 5-7 times a week	oral, three times a day	oral, once daily
Dosage (licensed age)	20-60mg/kg/day for <3 year old (max. 40mg/kg)	25mg/kg three times daily for aged ≥6 years	20-30mg/kg/day aged ≥ 2 years
Year on market	>40 years ago	Aug 1999 (2004 in HA)	Nov 2005 (2007 in HA)
Efficacy	- current standard iron chelator - improves hepatic, cardiac, and endocrine dysfunction	From Cochrane review - both deferiprone and desferrioxamine significantly reduced iron stores	- in randomised non-inferiority, phase 3 one-year multicentre open-label trial (n= 586):

	Desferrioxamine (Desferal®)	Deferiprone (Ferriprox®)	Deferasirox (Exjade®)
		- no evidence to suggest that either was more clinically efficacious.	52.9% deferasirox (oral 5-30mg/kg) versus 66.4% desferrioxamine(sc 20-60mg/kg 5 times per wk) responded to treatment.
		<u>From individual studies</u> - Deferiprone is comparable with desferrioxamine as monotherapy over a 1 year - deferiprone may remove myocardial iron more effectively than desferrioxamine - cardiac disease free survival over 5 years was more favourable with deferiprone versus desferrioxamine. - long-term studies show that liver iron is not adequately controlled by deferiprone monotherapy in a significant proportion of patient - anecdotal evidence of improved compliance in those who have difficulties with desferrioxamine but Cochrane review found no major differences in compliance between deferiprone & desferrioxamine (all achieved good to excellent compliance).	- indicating deferasirox may not have been as effective as desferrioxamine. - However, in sub-group analysis of the 381 pt who had particularly high levels of iron in the liver (Liver Iron Concentration >7mg Fe/g dry weight) at the start of study, including paediatrics at 30mg/kg/day receiving comparable doses of deferasirox or desferrioxamine, both medicines were as effective. - 20mg/kg/day deferasirox ↓ iron burden but this may not be comparable to reduction shown with desferrioxamine - no information on the effects of deferasirox on cardiac iron concentrations and dysfunction from large prospective randomised controlled studies - Deferasirox improves patient satisfaction and quality of life over desferrioxamine

	Desferrioxamine (Desferal®)	Deferiprone (Ferriprox®)	Deferasirox (Exjade®)
Long term efficacy	- lengthens survival	- no data on long-term outcomes (mortality and end organ damage)	- long term safety and efficacy of deferasirox is currently unknown.
Side effects	- common (>10%) side effects: local injection site disorder, arthralgia/myalgia - Growth retardation and bone changes may result from iron overload or excessive desferrioxamine dose :(1-10% in chelated patients given 60 mg/kg), esp. in children <3 year; but considerably less risk if ≤40 mg/kg. - Rare (0.01 to 0.1%): retinal abnormalities, vision loss, tinnitus and hearing loss - Very rare (≤0.01%): severe allergic reactions and thrombocytopenia	- common (≥10%) side effects: chromaturia (reddish brown urine), nausea, abdominal pain and vomiting. - -Arthropathy (>1 to ≤10%) ranged from mild pain in one or more joints to severe arthritis with effusion and significant disability. - Serious adverse effects: in trials :agranulocytosis (1.1%) and neutropenia (4.9%) - reversible neurological disorders on chronic overdose has also been reported. - From 1999 to Nov 2006, 46 cases of agranulocytosis associated with deferiprone have been identified. Of these 9 were fatal, 4/9 fatal cases occurred since Sept 2005 where advice given in Product Information has not been followed. 5/9 fatal cases were prescribed for off label use. In all fatal cases weekly White Blood Cells monitoring were missing. - reported finding during clinical trials of liver fibrosis has not been confirmed.	- Common side effects: skin rash (7%), gastrointestinal symptoms (26%). - ↑ serum creatinine (33%), - Uncommon (≥0.1% to <1%) high-frequency hearing loss and early cataracts . - in post marketing surveillance, there have been reports of acute renal failure, some with a fatal outcome and cytopenias, including agranulocytosis, neutropenia and thrombocytopenia in the US where some of the patients died. Although most of these patients had pre-existing haematologic disorders that are frequently associated with bone marrow failure, a contributory role for deferasirox cannot be excluded.

	Desferrioxamine (Desferal®)	**Deferiprone (Ferriprox®)**	**Deferasirox (Exjade®)**
HADF classification	General	Special	Self Financed Item
Daily Cost $ 20kg-60kg body weight	$21.2-$169.4	$42-$168	$174.6 to $814.8
Current no. of pt in HA	403	233	19
Total annual cost to HA if all existing patients switched to Deferasirox	$25.7m to $119.9m	$14.8m to $69.3m	$1.21m to $5.7m

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