Low molecular weight heparin (LMWH) within North Central London (NCL)

CONTENTS

1.0 INTRODUCTION

Low molecular weight heparins (LMWH) are widely used for the prevention and treatment of venous thromboses as well as a number of unlicensed indications. Some, patients may be discharged from secondary care whilst on prophylaxis or treatment dose LMWH.

This guidance document aims to:

- Outline the types of patient that are considered appropriate for primary care management within NCL
- Outline those patients where management should remain within secondary care
- Outline the monitoring required for LMWHs
- Highlight essential information that should be transferred between sectors, in line with NPSA requirements 2010[1] (e.g. indication, dose, weight, renal function, monitoring, duration of treatment)

As there are a number of LMWHs in use across the sector, this document is not intended to be a treatment dose prescribing guide; the relevant local Trust policies and standard reference sources (e.g. BNF) should be consulted accordingly. This document is applicable to all NHS Trusts, CCGs and GPs within the NCL Joint Formulary Committee umbrella. Organisations wishing to commission services from NCL providers will be expected to abide with the recommendations within this document.

Abbreviations:

- **Warfarin:** where stated, this includes the other vitamin K antagonists, acenocoumarol and phenindione
- **VKA**: vitamin K antagonists
- **HIT**: Heparin induced thrombocytopenia
- **AC**: Anticoagulation

2.0 THROMBOPROPHYLACTIC LMWH – prescribing and monitoring

2.1 Thromboprophylaxis - secondary care

For the indications below, secondary care should supply and (where appropriate) monitor the entire defined course of LMWH (up to 6wks or longer as appropriate[2]). ***NB: list is not exhaustive / exclusive***

Speciality	Indication	**Usual duration** (as per NICE[2] or local Trust guidelines). ***Assumes pt is back to baseline mobility****
Orthopaedics	Hip fracture surgery	28-35 days post-op
Orthopaedics	Hip replacement	28-35 days post op
Orthopaedics	Knee replacement	10-14 days post-op
Orthopaedics	Major limb fracture / pelvic fracture	At least 28-35 days
Orthopaedics	Lower limb plaster cast	For duration of plaster cast
Orthopaedics	Other high risk major orthopaedic surgery	Up to 6 weeks or as per orthopaedic surgeon *(NB: primary care may be asked to prescribe if thromboprophylaxis required beyond 6 weeks)*
All surgical specialities	Major cancer surgery in the abdomen or pelvis	28 days post-op
All surgical specialities	Higher VTE risk post-op (excludes patients usually on warfarin)	As directed by the surgeon / haematologist. Usually up to 28 days post-op
Bariatric surgery	Laparoscopic sleeve gastrectomy / gastric bypass / gastric band	At least 5-7 days post-op
Haematology / obstetrics	Higher VTE risk postnatally *(see section 2.2 re antenatal LMWH)*	Up to 6 weeks postnatally as per haematology consultant
Obstetrics	Intermediate VTE risk postnatally	At least 7 days post delivery[3] or as advised by haematology consultant. *NB prophylactic LMWH doses used in pregnancy differ from the usual licensed doses – see section 2.3*
Haematology	Higher VTE risk patient treated with VTE inducing drug such as lenalidomide/thalidomide	For duration of lenalidomide/thalidomide and as advised by haematology consultant
Oncology	High risk of VTE and receiving chemotherapy (e.g. previous PICC associated VTE)	As advised by oncologist / haematologist. Note: VTE risk continues whilst ongoing active cancer.

**Duration may need to be extended if not fully mobile*

2.2 Thromboprophylaxis - primary care

For the indications below, it is considered appropriate for primary care to supply/monitor LMWH for extended duration (> 6weeks), or for long-term thromboprophylaxis. Initial supply (e.g. 4wks) from secondary care. ***NB: list is not exhaustive/ exclusive***

Speciality	Indication	**Duration as per local specialist (or local Trust guidelines).**
Gastroenterology / Nutrition	History of PICC associated DVT and with a need for ongoing PICC line (e.g. for parenteral nutrition)	Whilst PICC line remains *in situ*
Orthopaedics	Complex orthopaedic surgery	As per orthopaedic surgeon on a case-by-case basis
Oncology	High risk of VTE and not receiving chemotherapy	As advised by oncologist / haematologist. *NB: VTE risk continues whilst ongoing active cancer*
Haematology/ obstetrics	Obstetric patient requiring thromboprophylaxis during pregnancy (e.g. for VTE / cardiac indications)	As advised by haemostasis/ haematology consultant *(UCLH pts will be managed in secondary care). See comment in section 2.3 re dose.*
Haematology	Higher risk patients as per haemostasis /haematology consultant	As advised by haemostasis / haematology consultant on a case-by-case basis
Haematology	Very high risk VTE pt requiring pre-flight VTE thromboprophylaxis – Haem advice only	Single doses pre-flight as advised by haemostasis / haematology consultant

2.3 Dose - thromboprophylaxis

If > 100kg use higher doses as per secondary care guidelines (not included)

LMWH	Prophylactic doses as per BNF
Dalteparin	2500 units or 5000 units sc OD
Enoxaparin	20mg or 40mg sc OD
Tinzparin	3500units or 4500 units sc OD

Dose (thromboprophylaxis) in PREGNANCY

- LMWH thromboprophylactic doses used in pregnancy differ to the standard doses listed in the BNF - the haemostasis/haematology consultant will advise accordingly.
- Patients > 90kg may require a higher thromboprophylactic dose as per RCOG[3], local guidelines and as advised by haemostasis/haematology consultant. Any potential dose changes based on weight, will be made clear in correspondence from the consultant

3.0 THERAPEUTIC DOSE LMWH – prescribing and monitoring

3.1 Therapeutic - secondary care

For the indications below, secondary care should prescribe / monitor therapeutic dose LMWH and make appropriate plans for follow up. ***NB: list is not exhaustive / exclusive.*** In some cases, LMWH may be split into two divided doses as advised by haematology.

Speciality	Indication	Usual duration (or as per local Trust guidelines)
AC clinic (hospital based)	Warfarin patient requiring a 'bridging' plan around surgery/procedure; patient's own AC clinic to organise and manage LMWH	Peri-procedurally and until INR back in range (*NB: some patients may receive thrombo-prophylactic rather than treatment dose)*
	Note: it is the duty of the surgical/medical team in charge of the patient's clinical care, to use local Trust bridging guidelines in liaison with both the patient's own AC clinic and pre-assessment clinical team, to formulate a pre-operative bridging plan. If there is a date change to the procedure, team to also communicate accordingly	
AC clinic (hospital based)	Patient in process of being newly warfarinised and LMWH being used as an interim	Until warfarinised as per local guidelines
Haematology	Pregnant women on therapeutic dose or higher intensity LMWH	Antenatally and postnatally, as per haemostasis / haematology consultant
Oncology	Patient requiring therapeutic dose LMWH and undergoing chemotherapy.	Depends on indication for anticoagulation. LMWH usually continues for duration of chemotherapy and in the case of new VTE for at least 6 months post event (whichever is the longer) and then oncology to review; if ongoing active cancer, then AC is usually continued beyond 6 months as ongoing VTE risk
Any speciality	Patients with history of recent bleed or bleeding disorder (e.g. thrombocytopenia) on anticoagulation	Follow up as per local trust arrangement; haemostasis/haematology consultant to define when patient can be transferred to Primary care.
Haematology	High risk VTE patient treated with VTE inducing drug such as lenalidomide or thalidomide	For duration of lenalidomide/ thalidomide and as advised by haematology consultant

3.2 Therapeutic - initial management by 2^0 care, before considering transfer to 1^0 care

- The following patient groups will initially be managed by the team in charge of the overall care of the patient with specialist haemostasis/haematology advice (preferably before discharge). ***NB: list is not exhaustive / exclusive.***
- If it is the intention that the GP should continue the prescribing and monitoring of LMWH, then the form in appendix 1 (*or a suitably detailed letter or discharge summary outlining similar information*) should be completed and faxed to the GP. This should be scanned onto the hospital electronic patient records, as proof of communication
- Clear instructions must be provided to the GP regarding when an adjustment to the LMWH dose would be required (e.g. weight change, change in renal function) – see section 4.0)
- In some cases, LMWH may be split into two divided doses as advised by haematology

Speciality	Patient groups		Comments
Any speciality	Renal impairment*: CrCL < 30mL/min: enoxaparin or dalteparin; CrCL < 20mL/min: tinzaparin		Dose reductions required for renal impairment as advised by haemostasis / haematology consultant
Any speciality	Significant hepatic impairment		
Any speciality	High body weight e.g. > 110 kg for dalteparin, > 105 kg for tinzaparin, > 100kg for enoxaparin	Or low body weight e.g. < 40kg	
Haematology	Ongoing LMWH monitoring and patient review by a haemostasis/haematology consultant, but where the ongoing prescribing of LMWH could be provided in primary care for patient convenience		These patients may have e.g. 3-6 monthly / annual follow-up with haematology and it is usually inappropriate to prescribe for these durations. 1^0 care may be asked to prescribe.
Any speciality	Patient requiring higher intensity anticoagulation (e.g. higher than standard BNF VTE dose) as advised by haemostasis/haematology consultant (example: dalteparin 120 units/kg sc BD)		Higher intensity for a period of time (patient specific) as defined by haemostasis / haematology consultant (follow up as per local trust arrangement)
Oncology	Whilst on chemotherapy, LMWH should be managed by secondary care. When chemotherapy has stopped, transfer to primary care could be considered.		Duration depends on indication and cancer status. First VTE event in setting of cancer: LMWH usually for at least 6 months then review by oncology; if ongoing active cancer, then AC is usually continued beyond 6months although choice/dose can be reviewed. Patient may require longterm LMWH

*could use eGFR in place of CrCL for *most adult patients of average build and height as per BNF*. **But**, for extremes of body weight, use CrCL (see comment in section 4.3 and appendix 2)

3.3 Therapeutic - primary care

For the following indications, it is considered appropriate for primary care to supply and monitor **therapeutic dose LMWH**. Initial supply is usually from secondary care. ***NB: list is not exhaustive / exclusive. GPs can prescribe and monitor for other patient groups if it is in the patient's best interest to do so***. In some cases, LMWH may be split into two divided doses as advised by haematology

Speciality	Indication	Usual duration* (or as per local Trust guidelines)
Any speciality	Unsuitable for warfarin or alternatives e.g. • Poor compliance (i.e. likely or proven non-clinic attendance e.g. IVDU, homeless etc) • Unable to attend AC clinic (housebound, bedbound) and with poor peripheral venous access (i.e. safety issue regarding monitoring) • Anticipated poor INR control or failure to achieve therapeutic anticoagulation on VKA • Intolerance to VKA or contraindication • Excess alcohol, binge drinking	For VTE, usually up to 6 months but may be longer as advised by haemostasis / haematology consultant
Any speciality	Defined course of anticoagulation (e.g. superficial thrombophlebitis, provoked calf or proximal DVT, line associated thrombosis etc) and where oral anticoagulation with VKA is not suitable for clinical reasons	The duration of anticoagulation needs to be clearly defined by secondary care
Any speciality	Warfarin patient requiring a 'bridging' plan around surgery or procedure and where the GP practice provides an AC service	This applies if the GP practice AC service includes 'bridging' anticoagulation, which should be in accordance with the relevant hospital's bridging guidelines. GP can refer to relevant anticoagulant clinic if needed.
	The pre assessment clinic may request that the GP prescribes 3-5 days of LMWH pre-op as part of the bridging plan. In such instances, the GP will be forwarded a patient specific plan and relevant guidelines as appropriate. *Note: it is the duty of the surgical/medical team in charge of the patient's clinical care, to use local Trust bridging guidelines in liaison with the patient's own AC clinic and pre-assessment clinical team, to formulate a pre-operative bridging plan. If there is a date change to the procedure, team to also communicate accordingly*	
Oncology	Patient does not require, or has completed chemotherapy and is no longer under the direct care of the oncologist , but requires ongoing LMWH	Duration depends on indication and cancer status. First VTE event in setting of cancer: LMWH usually for at least 6 months then review by oncology; if ongoing active cancer, then AC is usually continued beyond 6mths although choice and dose can be reviewed at that point. Patient may require longterm LMWH

3.4 Dose (therapeutic)

- The relevant local Trust policies and standard reference sources (e.g. BNF) should be consulted
- For patients of **high body weight** (e.g. > 110kg for dalteparin, > 105kg for tinzaparin or > 100kg for enoxaparin) or **low body weight** (e.g. < 40kg), seek advice from the local haemostasis SpR
- In some cases, LMWH may be split into two divided doses as advised by haematology
- **Antenatal / postnatal:** therapeutic / higher intensity dose LMWH will be as per haemostasis consultant
- **Oncology**: On occasions, the dose may be higher or lower than the standard weight based BNF dose. This may depend on whether the patient is at a higher risk of bleeding or requires high intensity LMWH. The haemostasis/haematology cons. will advise accordingly. If this occurs, then it should be clearly documented by secondary care.

4.0 MONITORING OF LMWH

In general and unless otherwise specified by secondary care, the following is advised:

4.1 MONITORING – therapeutic dose LMWH

Parameter	Comment
FBC, U&E and LFTs every 4 to 6 weeks (or as clinically indicated; maximum interval 3 months)	• Enoxaparin and dalteparin: review dose if estimated CrCL* falls to < 30mL/min. • Tinzaparin: review treatment dose if CrCL* falls to < 20mL/min • Discuss with haemostasis SpR if there is any significant change in renal function or if CrCL falls below the values above • Monitoring for HIT is not routinely required unless the risk is > 1% (see section 5.0)
Weight every 4-6 weeks or as clinically indicated (maximum interval 3 months)	• Dalteparin: adjust dose in line with the BNF weight bandings (or as advised by secondary care) • Tinzaparin / enoxaparin: review dose if weight changes by more than 5kg (or as advised by secondary care)

* could use eGFR in place of CrCL for *most adult patients of average build and height as per BNF*. **But** for extremes of body weight, use CrCL with caution (see section 4.3 and appendix 2)

4.2 MONITORING – thromboprophylactic dose LMWH

Parameter	Comment
Clinical monitoring is not required	Patient should be advised (with this advice documented), to report bleeding/bruising symptoms to his/her doctor
HIT monitoring is not routinely required unless the risk is > 1%	See section 5.0

4.3 COMMENT RE RENAL FUNCTION - eGFR vs CrCL

The BNF states the following:

- Renal function is measured either in terms of estimated glomerular filtration rate (eGFR) normalised to body surface area (BSA) 1.73m^2 or it can be expressed as creatinine clearance, often calculated from the Cockcroft & Gault (C&G) formula.
- In adults, renal function is increasingly being reported on the basis of eGFR (mL/min/1.73m^2). However, published information on the effects of renal impairment on drug elimination and manufacturer's dosing recommendations, are usually stated in terms of CrCL (C&G).
- Although eGFR and CrCL are not interchangeable, in practice and for *most adult patients of average build and height*, eGFR can be used to determine dose adjustments in place of CrCL.
- For patients at extremes of body weight (BMI < 18.5kg/m^2 or > 30kg/m^2) the *absolute* glomerular filtration rate* or CrCL (from C&G formula*) should be used to adjust doses. Note that there are inherent inaccuracies when estimating renal function in certain patient populations, such as the very elderly, reduced muscle mass, poor nutritional status or at extremes of body weight. It is advised that estimates are used with caution and dosing advice sought as appropriate from the local anticoagulation teams

*See appendix 2 for relevant calculations.

5.0 MONITORING FOR HIT (heparin induced thrombocytopenia)[5,6]

- The monitoring of HIT is only occasionally required and will affect relatively few patients
- **From a GP perspective, HIT monitoring (if indicated), amounts to one platelet check between days 4-7 post starting LMWH and once again between days 10-14, (assuming the patient is still on LMWH)**
- If HIT monitoring is required, secondary care should clearly document this on the discharge summary. Baseline platelet counts (i.e. pre LMWH) should be documented, as should any subsequent in-patient results. The discharge summary should be faxed to the GP as soon as possible pre-discharge with the monitoring requirement highlighted. The patient should be informed.
- Suspect HIT if platelets fall by 50% or more of pre-treatment baseline (even if the platelet count nadir remains above the lower limit of the normal range).
- In addition, consider whether HIT is a possible diagnosis if patient develops venous/arterial thrombosis or skin lesions at heparin injection sites.
- If HIT is suspected, **stop LMWH and urgently contact the local haemostasis SpR for advice.**

Recommendations for platelet monitoring (based on ACCP 2012[5] and BCSH 2012[6] recommendations)

Secondary care should use this table to identify those patients requiring HIT monitoring. If this is required on discharge, then the secondary care team should ensure that the GP is notified accordingly

Patient type	Platelet monitoring for HIT
LMWH only (prophylactic or therapeutic) **and** where: 1. the risk of HIT is < 1% (see incidence table below) **AND** 2. pt does not fall into the other heparin categories below	• Baseline platelet count • Subsequent monitoring not required i.e. HIT monitoring is not required for all medical, obstetric and surgical patients (including orthopaedic). ***Exception:*** cardiothoracic surgery (where the incidence of HIT is 1-3%) and cancer patients undergoing surgery (where the risk of HIT is unclear but likely to be at least 1%).
LMWH and HIT incidence > 1% (see incidence table below)	• Baseline platelet count • Once between days 4-7 post starting LMWH • Once again between days 10-14 whilst on LMWH
UFH (unfractionated heparin) during the current in-patient episode and now on LMWH	• Baseline platelet count • Once between days 4-7 post starting UFH and • Once again between days 10-14 whilst on LMWH
ANY type of heparin within the previous 100 days	• Baseline platelet count • Check at 24 hours • Thereafter as per other categories as appropriate
UFH (unfractionated heparin) infusion	• Baseline platelet count • Check at 24 hours if UFH/LMWH has been administered within the previous 100 days • Every 2-3 days from days 4-14 or until UFH is stopped (whichever occurs first)

Incidence of HIT according to patient population and type of heparin exposure (ACCP 2012[5])

Patient population (min. of 4days exposure)	Incidence of HIT	Patient population (min. of 4days exposure)	Incidence of HIT %
Post-operative patients		**Medical**	
Heparin prophylactic dose	1-5%	Cancer	1%
Heparin therapeutic dose	1-5%	Heparin prophylactic of therapeutic dose	0.1-%1
Heparin flushes	0.1-1%	LMWH prophylactic or therapeutic dose	0.6%
LMWH prophylactic of therapeutic dose	0.1-1%	ITU patients	0.4%
Cardiac surgery patients	1-3%	Heparin flushes	< 0.1%
		Obstetric patients	< 0.1%

6.0 IN-PATIENT DISCHARGES FROM SECONDARY CARE

- The discharging team must ensure that the patient receives uninterrupted anticoagulation therapy (usual minimum of 2 weeks supply) until the patient can be reviewed by the GP or hospital clinic, whichever has been agreed. Note that some patient groups who will be managed by primary care (e.g. homeless, IV drug misusers), may not be safe for a 2 week supply. In these cases, dialogue with the GP pre discharge is required and early GP follow-up organised
- If a finite period of *thromboprophylaxis* is required and it is clinically appropriate to do, then the entire quantity of LMWH can be supplied on discharge (e.g. up to 6 weeks)
- The discharging team must also ensure that the patient or a relative is able to administer LMWH, otherwise referral to a district nurse should be made. For out of area patients, if self administration or district nurses are not viable options, then consideration should be given to Homecare services.
- A yellow sharps bin should also be provided by secondary care
- **Clear documentation regarding anticoagulation management, MUST be included on discharge paperwork from secondary care** (see section 7.0)
- The GP may occasionally be required to undertake HIT monitoring (section 5.0). In these cases secondary care should clearly document this on the discharge summary. Baseline platelet counts (i.e. pre LMWH) should be documented, as should any subsequent in-patient results. The discharge summary should be faxed to the GP as soon as possible pre-discharge with the monitoring requirement highlighted. The patient should be informed.
- If it is the intention that the GP should continue the prescribing and monitoring of LMWH, then the form in appendix 1 (*or a suitably detailed letter or discharge summary outlining similar information*) should be completed and faxed to the GP

7.0 INFORMATION PROVISION - between secondary and primary care (and *vice versa*)

For all transfers of care between primary/secondary care and *vice versa*, it is expected that the following information should be included on relevant paperwork. This is in line with good practice as per the NPSA[1].

- Indication for anticoagulation
- Dose prescribed including intentional dose adjustments and rationale where appropriate
- Approximate start date and expected duration of therapy
- Who is responsible for clinical review and when
- Most recent weight in kg (with date) and an 'alert' weight (where LMWH dose adjustment needed)
- Baseline and recent blood results (e.g. Hb, platelets, serum creatinine)
- Renal function (section 4.3)
- Requirements for ongoing monitoring (section 4.0), including platelet monitoring for HIT if appropriate (section 5.0)
- Who is responsible for prescribing and monitoring
- Any additional relevant information (e.g. district nursing services required, patient self-administering)

References

1. NPSA, National Patient Safety Agency Rapid Response Report (RRR 014): Reducing treatment dose errors with low molecular weight heparins. July 2010
2. NICE clinical guideline 92 **Venous thromboembolism: reducing the risk** http://www.nice.org.uk/nicemedia/live/12695/47197/47197.pdf
3. Royal College of Obstetricians and Gynaecologists (RCOG) Green top guideline 37a: Reducing the risk of thrombosis and embolism during pregnancy and the puerperium. Nov 2009. http://www.rcog.org.uk/files/rcog-corp/GTG37aReducingRiskThrombosis.pdf
4. British national Formulary No 66. BMJ Group and the Pharmaceutical Press; London
5. Linkins et al. American College of Chest Physicians. Treatment and prevention of heparin induced thrombocytopenia: antithrombotic therapy and prevention of thrombosis 9th edition. ACCP clinical practice guidelines. *Chest* 2012; 141;e495S-e530S
6. Watson et al. BCSH Guidelines on the diagnosis and management of heparin induced thrombocytopenia: second edition. 2012; http://www.bcshguidelines.com/4_HAEMATOLOGY_GUIDELINES.html

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Appendix 1: LMWH transfer to primary care within NCL

NHS Trust logo here

Secondary care: To complete this form OR to ensure that all information is included in a discharge summary or an out-patient letter to the GP

Consultant: …… Speciality: …… Clinic date: ……	Hospital Address
Patient name: DOB: Hospital No:	Patient's address
Dear Doctor ……	GP details

The above patient requires ongoing subcutaneous treatment with …… injection, for the indication as outlined below. We have supplied ……days of therapy on …….. and would be grateful if you could please continue to supply and monitor thereafter.

Indication	Wt(Kg)+ date	Height + date	Dose & frequency	Std BNF dose? Y / N

Details of individualised dosing, if standard weight based BNF dosing not applicable:

Start date:	Hb (date)	Plts (date)	Serum Cr (date)	CrCL (mL/min)	eGFR (mL/min/1.73m^2)

Proposed duration	Date for review

Responsibility for reviewing AC

Other relevant conditions

Standard LMWH monitoring (unless otherwise advised):

- FBC, U&E and LFTs every 4 to 6 weeks (or as clinically indicated, max. interval 3mths). Seek advice from haem SpR if renal function significantly deteriorates or if CrCL/eGFR <30mL/min with enoxaparin /dalteparin or CrCL/eGFR < 20mL/min with tinzaparin *(see section 4.3 of NCL LMWH document regarding eGFR/CrCL).*
- Check weight every 4-6 wks or as clinically indicated, max 3mthly. Tinzaparin/enoxaparin: review dose if > 5kg weight change. Dalteparin: review dose in line with BNF weight bandings.

Additional specific monitoring for this patient:

Additional comments (including administration details if applicable):

Thank-you for following up. If you wish to discuss further, please contact using the details below.

Yours sincerely:……Print: ……

Grade…… Contact details: ……Date ……

Confidentiality info

Appendix 2: Cockcroft-Gault and Absolute GFR

Cockcroft & Gault (C&G) Formula	
Estimated CrCL (mL/min)	= $\frac{(140\text{-age}) \times \text{weight} \times \text{constant}}{\text{Serum Cr}}$

- Age in years
- Weight in Kg (ideal bodyweight but see below)
- Serum Creatinine in micromole/L
- Constant = 1.23 (male) or 1.04 (female)

Estimated ideal body weight (IBW) kg

- Males: IBW = 50 kg + 2.3 kg for each inch over 5 feet
- Females: IBW = 45.5 kg + 2.3 kg for each inch over 5 feet

- If total body weight (TBW in Kg) is ≤ 120% IBW, then use TBW in C&G formula
- If total body weight (TBW in kg) is > 120% IBW, then calculate and use adjusted body weight (ABW in Kg) in C&G formula
- ABW = IBW + [0.4 x (TBW-IBW)]

Absolute Glomerular Filtration Rate	
Actual GFR	= eGFR x (patient's BSA /1.73)

- BSA = Body surface area (formulas available via Internet)

Bibliography

Cockcroft DW and Gault H. Prediction of creatinine clearance from serum creatinine. Nephron 1976;16: 31-41.
Basic Clinical Pharmacokinetics 4th edition; 2004. Michael Winter. Editor: DB Troy. Lippincott Williams& Wilkins, Philadelphia