



Reference : Recombinant Activated Factor Seven
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CIRCULAR 28 of 2011: USE OF RECOMBINANT ACTIVATED FACTOR VII IN INTRACTABLE BLEEDING

Circular 11 of 2011 included a draft guideline on the use of rFVIIa for comments. Submissions on the draft guideline were considered by the CMS and were discussed at an open meeting with affected stakeholders on 18 April 2011. These submissions are available on the CMS website¹.

After considering the concerns of all the stakeholders, reviewing the available evidence CMS has concluded that in general, the use of rFVIIa in intractable bleeding does not meet the criteria to qualify as treatment in managing intractable bleeding as an emergency in accordance with the PMB regulations.

The code of conduct² requires that benefit definitions must:

- i. consider the level of appropriate clinical practice as desired in the public sector,
- ii. be supported by well researched evidence based clinical protocols, formularies or treatment guidelines,
- iii. must be based on repeatable procedures that have demonstrated significantly improved clinical outcomes,
- iv. must have been tested on large numbers of people,
- v. must represent a high level of agreement among academic health professionals

The use of rFVIIa fails to meet the above criteria since evidence is inadequate, some reports indicate some benefits, some report adverse outcomes, and others indicate no benefits at all.

¹ Submissions on the draft rFVIIa guideline in intractable bleeding, available under the PMB definition project at [http://www.medicalschemes.com/Publications.aspx?id=43&category=PMB Definition Project](http://www.medicalschemes.com/Publications.aspx?id=43&category=PMB%20Definition%20Project)

² Code of Conduct in respect of PMB benefits, 31 July 2010, available at: http://www.medicalschemes.com/files/Guidelines%20and%20Manuals/CodeOfConduct_20100803.pdf

In spite of the absence of convincing evidence, there is some anecdotal evidence, and eminent professional opinions, which indicate that rFVIIa may be useful in a selected group of patients who have been adequately treated with the appropriate blood transfusion protocols and who have an increased “R” time. In view of this, the CMS will continue to adjudicate on complaints related to the use of rFVIIa on case by case basis, considering the clinical situation and other merits of individual cases. The previously published draft guideline will however not be published as a benefit definition.

A handwritten signature in black ink, appearing to read 'Boshoff Steenekamp', with a long horizontal stroke extending to the right.

Boshoff Steenekamp

Strategic Projects Specialist



MINUTES OF THE MEETING FOR THE MEETING TO DISCUSS THE rFVIIa USAGE IN INTRACTABLE BLEEDING

Date: 18 April 2011

Time: 14h00-16h45

Venue: Council of Medical schemes ULWAZI

Attendance:

Boshoff Steenekamp (CMS, Chairperson))
Ephraim Akpalu (Mamelodi Day hospital)
Hasina Cassim (Discovery)
Prof Johnny Mahlangu (Wits, Haematology Association, MASAC)
Prof Ken Boffard (Wits, Trauma Association)

Margaret Campbell (Discovery)
Philemon Masopha (Qualsa)
Selaelo Mametja (CMS)
Stan Moloabi (GEMS)
Stephen Rich (Discovery)
Sylvia Cornejo-Vega (Discovery)

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1 Opening and Background

- 1.1 Boshoff opened the meeting and indicated that Council had received a number of complaints in respect of rFVIIa usage where claims were not paid by schemes, and that a scheme has requested Council to consider the matter because it appeared that there might be a flood of off-label use of the drug under clinical conditions that did not warrant its use.
- 1.2 The CMS viewed the development of an rFVIIa guideline as a benefit definition (BD), which must meet the criteria for BDs as defined in the July 2010 code of conduct in respect of PMB benefits.
- 1.3 The development of Benefit Definitions is part of Council's role in protecting beneficiaries, to prevent beneficiaries from incurring costs when medical schemes do not pay in circumstances where expensive drugs were used which may not meet the affordable, cost effectiveness, and evidence based criteria as stipulated in the code of conduct. The purpose of BDs is to improve clarity and to prevent complaints, thus forming part of prospective regulatory activities by the CMS.
- 1.4 CMS developed the guideline as a BD, since rFVIIa is used mainly in emergency circumstances, and frequently meets the criteria for a PMB as described in the regulations as "any medical emergency".
- 1.5 The CMS presented a draft a guideline, which was based on the International Trauma Association guideline and the draft Medical and Scientific Advisory Council (MASAC) of the South African Haemophilia Foundation, which was kindly edited by Professors Mahlangu and Boffard before publication.
- 1.6 The following concerns were raised by the delegates:
 - 1.6.1 Concerns surrounding the off -label use of rFVIIa
 - 1.6.2 The role medical schemes representative argued that CMS has no developing clinical guidelines
 - 1.6.3 The lack of evidence for the use of rFVIIa
 - 1.6.4 The absence of other providers at the meeting

2 Considerations of Submissions

2.1 Medscheme submission

- 2.1.1 The meeting was concerned about the lack of evidence supporting use of rFVIIa in intractable bleeding and the actual costs of treating a patient, it was estimated that for an 80kg adult the cost will be around R167,000
- 2.1.2 The meeting agreed that the evidence supporting rFVIIa is very weak indeed. The studies are mostly measure the reduction of blood products used as an endpoint, and mortality reduction data is scanty.
- 2.1.3 Professor Boffard, who was involved in an initial study, indicated that it was difficult to recruit enough cases to have a powerful study. At the design phase of the study the mortality rate was estimated at 30%, however interim analysis reported a mortality rate of 8% amongst the study groups. The drug company required a study population size of 4500, which proved to be expensive for the company and therefore terminated the study based on economical feasibility of the study.
- 2.1.4 Professor Boffard also indicated that there are positive results in the military setting, however there were concerns regarding application of such findings in non-military populations.

2.2 V-Med submission

- 2.2.1 V-Med was concerned about jurisdiction of the council regarding development of protocol, the off-label use of rFVIIa and inconsistent approach of developing guidelines.

2.3 Discovery submission

- 2.3.1 Discovery was mainly concerned about off label use of the drug, lack of robust evidence, costs and management of costs associated with the drug.
- 2.3.2 Discovery was also concerned about the contents of the protocol such as lack of references, contraindications and cost consideration.




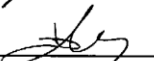
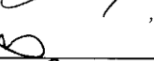
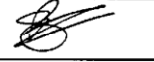


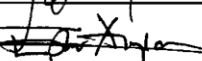
3 Discussion of the contents of the protocol and its application

- 3.1 It was indicated that this drug only works in a clearly defined subset of patients, who have increased R time on TEG and have not responded to the full massive transfusion protocol.
- 3.2 There were concerns that in a practical setting the physicians may not be able to collect all the blood test required in order to select patients who will definitely benefit from the drug. Whilst TEG is the standard in diagnosing definitive deficiencies in coagulopathies, it is not widely available. It costs around R450.00 to do a TEG. Not using a TEG but clinical presentation may results in many false positives therefore increasing inappropriate use of the drug
- 3.3 There was a concern that inappropriate use of rFVIIa may be due to lack of extensive knowledge of massive transfusion protocol, and it was suggested that the rFVIIa protocol should not be circulated on its own, but as part of massive transfusion protocol
- 3.4 There were discussion on cost of this drug especially associated with massive doses and that the costs may not be affordable to majority of schemes.

4 Conclusion

- 4.1 The CMS indicate that it would consider the discussions of this meeting before taking any further steps in publishing a guideline. It may be necessary to have further discussions with the DoH, the MCC (regarding off-label use of rFVIIa) and the HPCSA (regarding use of drugs which are costly and not part of schemes protocol when the practitioner are well aware of the fact).
- 4.2 The delegates of the meeting could not reach a consensus on use of rFVIIa. The scheme representative indicated that rFVIIa should not be used as part of the protocol of the Massive transfusion; CMS indicated that until the matter is resolved, adjudication of complaints will consider merits of each case.

Attendance register

18 April 2011 Guideline on the use of Recombinant Factor Meeting			
Name	Email	Tel/Mobile	Signature
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