Allegato al Decreto del Commissario ad ACTA

n. 109/2016 del 28 SET. 2016

POLITICHE DELLA SALUTE - IL COMMISSARIO AD ACTA

ALLEGATO A

Revisione della letteratura

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Regione Abruzzo Dipartimento per la Salute e il Welfare

Tabella 1 – Riassunto dei principali risultati della revisione sistematica e metanalisi *"Penny F. Whiting; Robert F.Wolff; Sohan Deshpande, et al. Cannabinoids for Medical Use A Systematic Review and Meta-analysis*. JAMA 2015; vol 313 (24): 2456-2473" per indicazione terapeutica.

GLAUCOMA

Un solo clinical trial crossover ha confrontato THC (5mg), cannabidiolo (20 mg), cannabidiolo spray oromucosale (40 mg) e placebo. I risultati non hanno mostrato alcuna differenza tra il placebo e i cannabinoidi sui valori della pressione intraoculare.

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SINDROME DE LA TOURETTE

Due piccoli studi controllati verso placebo (4 reports; 36 partecipanti) suggeriscono che il THC può essere associato a un miglioramento significativo della severità dei TIC nei pazienti con Sindrome de La Tourette.

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SPASTICITÀ DOVUTA A SCLEROSI MULTIPLA (SM) O PARAPLEGIA

'14 studi (33 reports; 2280 partecipanti) hanno valutato la spasticità dovuta a SM o paraplegia. 11 studi (2138) hanno incluso pazienti con SM e 3 pazienti con paraplegia (142 partecipanti) causati da traumi al midollo spinale. 6 studi hanno valutato "nabiximols", 3 dronabinolo, 1 nabilone, 4 THC /CBD (2 di questi anche il dronabinolo) 1 ciascuno per ECP002A e THC fumata. Tutti gli studi erano verso placebo nessuno vs un comparator attivo. Due studi erano a basso rischio di bias, 5 a rischio non chiaro di bias e 7 ad alto rischio di bias. Gli studi suggeriscono che i cannabinoidi sono associati a miglioramenti della spasticità, ma senza raggiungere la significatività statistica in molti studi. Non c'erano differenza chiare nel tipo di cannabinoide. Solo gli studi nei pazienti con SM avevano dati sufficienti a generare stime conclusive. I cannabinoidi sono associati con un miglioramento maggiore nella scala di Ashworth per la spasticità rispetto al placebo, anche se non in maniera statisticamente significativa. Sono inoltre associati a un miglioramento medio della spasticità su scale numeriche.

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NAUSEA E VOMITO DA CHEMIOTERAPIA

28 studi hanno valutato nausea e vomito da chemioterapia. 14 studi hanno valutato il nabilone e 3 il dronabinolo, 1 "nabiximols", 4 levonantradol, 6 THC. Due studi includevano anche una combinazione di dronabinolo con ondansetron e proclorperazina. 8 studi erano vs placebo, 3 verso un comparator attivo. I comparator attivi più comuni erano proclorperazina (15 studi), clorpromazina (2 studi) e domperidone (2 studi). Altri comparator (alizapride, idroxizina, metoclopramide e ondansetron) sono stati valutati in singoli studi. Dei 28 studi, 23 erano ad alto rischio di bias, non chiaro per 5. Tutti gli studi suggeriscono un maggiore beneficio dei cannabinoidi rispetto ai comparator attivi e al placebo, ma non si raggiunge la significatività statistica in nessuno.

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DOLORE CRONICO

E' stato valutato in 28 studi l'effetto dei cannabinoidi sul dolore cronico (63 report; 2454 partecipanti): 13 hanno valutato i "nabiximols", 4 THC fumata, 5 nabilone, 3 THC per via oromucosale, 2 dronabinolo, 1 cannabis vaporizzata (includendo 2 dosi), 1 capsule di acido ajulemico e 1 THC orale. Un trial ha confrontato il nabilone con l'amitriptilina; tutti gli altri studi erano verso placebo.

Le condizioni che causano dolore cronico variano tra gli studi e includono dolore neuropatico (centrale, periferico, o non specificato in 12 studi), 3 dolore oncologico, 3 neuropatia periferica diabetica, 2 fibromialgia, 2 neuropatie sensoriali HIV-associate, 1 studio per ciascuna delle seguenti indicazioni: dolore refrattario nella SM o altre patologie neurologiche, nella artrite reumatoide, nel dolore non-oncologico (nocicettivo e neuropatico), nel dolore centrale, nei problemi muscoloscheletrici, e nel dolore indotto da chemioterapia.

Due studi erano a basso rischio di bias, 9 a rischio non definito, e 17 ad alto rischio. Gli studi suggeriscono miglioramenti del dolore associati all'uso dei cannabinoidi ma senza raggiungere la significatività statistica in molti studi. Il numero medio di pazienti che ha riportato una riduzione del dolore di almeno il 30% era maggiore nel gruppo a cui erano somministrati cannabinoidi rispetto al placebo (OR 1.41 [IC 95% 0.99-2.00]. Un trial ha valutato il THC fumato e ha riscontrato i maggiori benefici (OR 3,43 [IC 95% 1.03-11.48] e 7 trial hanno valutato "nabiximols". In questi studi è stato valutato l'effetto su dolore neuropatico (OR 1.38 [IC95%0.93-2.03]; 6 trial) e dolore oncologico (OR 1.412 [IC95% 0.99-2.00]; 2 trial) senza differenze chiare tra le tipologie di dolore.

"Nabiximols" è anche associato con una riduzione media maggiore nel Numerical Rating Scale valutazione del dolore (differenza media pesata (WMD), -0.46 [IC 95% -0.80 a -0.11]; 6 trial), short form breve per la valutazione del dolore, indice complesso di severità (WMD, -0.17 [IC95%, -0.50 a 0.16]; 3 trial), dolore neuropatico (WMD, -3.89 [IC 95% -7.32 a -0.47]; 5 trial) e la proporzione di pazienti riportanti miglioramenti su una impressione globale di cambio di punteggio (OR 2.08 [IC 95%, da 1.21 a 3.59]; 6 trial) in confronto a placebo. Ci sono alcune evidenze a supportare questi dati ma non sono consistenti nei vari trial. Non c'è differenza nella media di punteggi di qualità di vita misurati con l'indice di stato di salute EQ-5D (WMD, -0.01 [IC95%, -0.05 to 0.02]; 3 trial) tra nabiximols e placebo. Due degli studi inclusi nella metanalisi per il NRS (scala da 0 a 10) hanno valutato pazienti con dolore oncologico, tutti gli altri studi hanno valutato il dolore neuropatico.

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STIMOLAZIONE DELL'APPETITO IN PAZIENTI CON HIV

4 studi hanno valutato la stimolazione dell'appetito in pazienti con infezione HIV /AIDS (4 reports; 255 partecipanti). Tutti gli studi hanno valutato dronabinolo, 3 vs placebo e 1 vs megastrol acetato. Ci sono alcune evidenze che il dronabinolo sia associato con aumento di peso rispetto al placebo. Evidenze più limitate che sia anche associato ad aumento di appetito, aumento massa grassa, riduzione di nausea, e miglioramento dello stato funzionale. Sono singoli studi che però non raggiungevano significatività statistica

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/A lo al Decreto del Commissario
a TA
n. 109/2016 del 28 SET. 2016

ALLEGATO B

Progetto pilota statale per la cannabis ad uso medico

Scheda per la raccolta dei dati dei pazienti trattati con *Cannabis*

Regione _____ ASL _____

MEDICO PRESCRITTORE

Nome _____ Cognome _____

Recapito telefonico _____ Indirizzo mail _____

☐ medico ospedaliero/specialista ☐ MMG

specializzazione *(specificare)* _____

PAZIENTE

Codice alfanumerico _____ Età *(anni)* ☐☐ sesso M F

(ai sensi art.5 comma 3 legge 94/98)

PRESCRIZIONE

☐ Cannabis FM2 ☐ Cannabis FM19 ☐ Importazione *(specificare)* _____

Data inizio terapia ☐☐☐☐☐☐☐☐ Durata terapia *(giorni)* ☐☐☐

Posologia in peso di cannabis

Dose die _____

N. somministrazioni / die _____

Modalità di assunzione

☐ orale ☐ inalatoria

☐ altro *(specificare titolo e dosaggio)* _____

_____

Esigenza di trattamento

☐ analgesia in patologie che implicano spasticità associata a dolore (sclerosi multipla, lesioni del midollo spinale) resistente alle terapie convenzionali

☐ analgesia nel dolore cronico (con particolare riferimento al dolore neurogeno) in cui il trattamento con antinfiammatori non steroidei o con farmaci cortisonici o oppioidi si sia rivelato inefficace

☐ effetto anticinetosico ed antiemetico nella nausea e vomito, causati da chemioterapia, radioterapia, terapie per HIV, che non può essere ottenuto con trattamenti tradizionali

☐ effetto stimolante dell'appetito nella cachessia, anoressia, perdita dell'appetito in pazienti oncologici o affetti da AIDS e nell'anoressia nervosa, che non può essere ottenuto con trattamenti standard

☐ effetto ipotensivo nel glaucoma resistente alle terapie convenzionali

☐ riduzione dei movimenti involontari del corpo e facciali nella sindrome di Gilles de la Tourette che non può essere ottenuta con trattamenti standard

☐ altro *(specificare)* _____

_____

TERAPIA ☐ Prima prescrizione ☐ Prosecuzione terapia ☐ Sospensione terapia

Prosecuzione della terapia ☐ sintomatologia migliorata ☐ sintomatologia stabile

Sospensione della terapia ☐ sintomatologia peggiorata ☐ comparsi effetti indesiderati ☐ sintomatologia stabile

Data sospensione terapia ☐☐☐☐☐☐☐☐

Impiego attuale della cannabis ☐ sostituisce terapia convenzionale ☐ integra terapia convenzionale

Regione Abruzzo Dipartimento per la Salute e il Welfare

SEZIONE DA COMPILARE SOLO ALLA PRIMA PRESCRIZIONE

Terapia convenzionale

- ☐ il trattamento precedente non ha prodotto gli effetti desiderati
- ☐ il trattamento precedente ha provocato effetti indesiderati non tollerabili
- ☐ il trattamento necessita di incrementi posologici che potrebbero superare la dose terapeutica
- ☐ altro *(specificare)* _____

_____

Paziente già in trattamento con prodotti a base di cannabis

Prodotto _____

posologia _____

Data dell'ultima assunzione di cannabis |_|_|_|_|_|_|_|_|

Durata del trattamento ☐ < 6 mesi ☐ 6-12 mesi ☐ > 12 mesi

- ☐ il trattamento ha migliorato la sintomatologia
- ☐ il trattamento non ha modificato la sintomatologia
- ☐ il trattamento ha peggiorato la sintomatologia
- ☐ sono comparsi effetti indesiderati

Nel caso in cui si osservi una sospetta reazione avversa, si ricorda di compilare la scheda di segnalazione (Allegato B del DM 9.11.2015) scaricabile dal sito www.epicentro.iss.it/focus/erbe/fitosorveglianza.asp

Osservazioni del medico prescrittore _____

_____

_____

_____

_____

_____

_____

_____

Timbro SSN *(se convenzionato)*

Luogo _____ data |_|_|_|_|_|_|_|_|

Istruzioni per la compilazione

Secondo quanto previsto dal Decreto del Ministero della salute 9 novembre 2015, al momento della prescrizione, il medico compila la Scheda per la raccolta dei dati dei pazienti trattati con *Cannabis* e la invia alla ASL territorialmente competente secondo le indicazioni che le stesse Regioni forniranno.
Il medico prescrive la preparazione magistrale secondo la normativa vigente, con particolare riferimento all'art. 5 della legge 94/98.

Allegato al Decreto del Commissario ad ACTA

n. 109/2016 del 28 SET. 2016

ALLEGATO C

Prescrizione preparazioni magistrali a base di Cannabis sativa

ASL:	Centro Prescrittore:
Codice Medico:	Recapito telefonico:
Codice Paziente:	
ASL residenza:	Data prescrizione:

Prescrizione

	Materia Prima	Cartine	Olio
	CANNABIS FLOS 19% THC (Bedrocan®)		
	CANNABIS FLOS 6% THC, 8% CBD (Bediol®)		
	CANNABIS FLOS <1% THC, 9% CBD (Bedrolite®)		
	FM 2 – Istituto Chimico Farmaceutico, Firenze		
	FM 19 - Istituto Chimico Farmaceutico, Firenze		

Posologia

Cartine		
Quantitativo (mg) di una singola cartina	Numero Cartine	Quantitativo totale (mg)

Modalità di assunzione

1 cartina ……volte al dì (dose/die) per via orale o inalatoria

Olio	
Quantitativo in grammi in 1 ml di olio d'oliva	
Estrazione oleosa secondo la metodica indicata nell'articolo scientifico pubblicato da Luigi L. Romano e Arno Hazekamp, 2013 – Protocollo 5	

Modalità di assunzione

Numero gocce: ….. pure o diluite …. volte al dì per via orale

Regione Abruzzo Dipartimento per la Salute e il

Motivo della prescrizione

Indicazioni terapeuiche a carico del SSR	
	Riduzione del dolore associato a spasticità (sclerosi multipla, lesioni del midollo spinale) con resistenza alle terapie convenzionali in pazienti affetti da sclerosi multipla con punteggio scala NRS ≥ 5
	Riduzione del dolore cronico (con particolare riferimento al dolore neurogeno, esclusa la fibromialgia) in pazienti con resistenza a trattamenti convenzionali (come da linee guida delle principali Società Scientifiche) e punteggio scala NRS ≥ 6
	Riduzione dei movimenti involontari del corpo e facciali nella sindrome di Gilles de la Tourette che non puo' essere ottenuta con trattamenti standard
Altre indicazioni terapeutiche approvate dal Ministero della Salute	
	Analgesia in patologie che implicano spasticita' associata a dolore (sclerosi multipla, lesioni del midollo spinale) resistente alle terapie convenzionali (anche con punteggio scala NRS <5)
	Analgesia nel dolore cronico (con particolare riferimento al dolore neurogeno) in cui il trattamento con antinfiammatori non steroidei o con farmaci cortisonici o oppioidi si sia rivelato inefficace (anche con punteggio scala NRS <6)
	Effetto anticinetosico ed antiemetico nella nausea e vomito, causati da chemioterapia, radioterapia, terapie per HIV, che non puo' essere ottenuto con trattamenti tradizionali
	Effetto stimolante dell'appetito nella cachessia, anoressia, perdita dell'appetito in pazienti oncologici o affetti da AIDS e nell'anoressia nervosa, che non puo' essere ottenuto con trattamenti standard
	Effetto ipotensivo nel glaucoma resistente alle terapie convenzionali

Timbro e Firma del Medico Prescrittore

PARTE RISERVATA ALLA FARMACIA

Prep. N°.	
Data di scadenza	
Data di consegna	
Costo della preparazione galenica	€

Timbro e Firma Farmacia

Reso cartine non utilizzate N°..... Data:.....

Motivazione:.....

Regione Abruzzo Dipartimento per la Salute

Allegato al Decreto del Commissario ad ACTA

n. 109/2016 del 28 SET. 2016

ALLEGATO D

Ministero della Salute | Istituto Superiore di Sanità | Agenzia Italiana del Farmaco

SCHEDA DI SEGNALAZIONE DI SOSPETTA REAZIONE AVVERSA A PRODOTTI A BASE DI PIANTE OFFICINALI E A INTEGRATORI ALIMENTARI

INFORMAZIONI SUL PAZIENTE

1. INIZIALI	2. ETA'	3. SESSO	4. PESO CORPOREO	5. ORIGINE ETNICA

6. EVENTUALE STATO DI GRAVIDANZA ☐ NO ☐ SI _____ settimana
ALLATTAMENTO ☐ NO ☐ SI

7. DATA INSORGENZA REAZIONE

8. DESCRIZIONE DELLA REAZIONE ED EVENTUALE DIAGNOSI

11. LA REAZIONE È MIGLIORATA CON LA SOSPENSIONE?
☐ NO ☐ SI

12. E' STATA ESEGUITA TERAPIA SPECIFICA?
☐ NO ☐ SI QUALE? _____

9. EVENTUALI ESAMI STRUMENTALI E/O DI LABORATORIO RILEVANTI:

13. GRAVITÀ DELLA REAZIONE
☐ OSPEDALIZZAZIONE
☐ INVALIDITÀ GRAVE O PERMANENTE
☐ PERICOLO DI VITA
☐ MORTE

14. ESITO
☐ RISOLUZIONE COMPLETA
☐ RISOLUZIONE CON POSTUMI
☐ REAZIONE PERSISTENTE
☐ MORTE

10. COMMENTI SULLA RELAZIONE TRA PRODOTTO E REAZIONE
☐ CERTA ☐ PROBABILE ☐ POSSIBILE ☐ DUBBIA ☐ SCONOSCIUTA

INFORMAZIONI SUL PRODOTTO

15. PRODOTTO SOSPETTO
(indicare la denominazione e la composizione come descritte in etichetta)

15-*a* QUALIFICA DEL PRODOTTO
☐ GALENICO ☐ PRODOTTO ERBORISTICO ☐ INTEGRATORE
☐ ALIMENTO ☐ ALTRO: _____

15-*b* PRODUTTORE

16. DOSAGGIO / DIE	17. VIA DI SOMMINISTRAZIONE	18. DURATA DELL'USO DAL AL	19. RIPRESA DELL' USO ☐ SI ☐ NO RICOMPARSA DEI SINTOMI ☐ SI ☐ NO

20. INDICAZIONI O ALTRO MOTIVO PER CUI IL PRODOTTO È STATO ASSUNTO O PRESCRITTO

21. FARMACO(I) CONCOMITANTE(I), DOSAGGIO, VIA DI SOMMINISTRAZIONE, DURATA DEL TRATTAMENTO

22. USO CONCOMITANTE DI ALTRI PRODOTTI *(specificare)*

23. CONDIZIONI CONCOMITANTI E PREDISPONENTI

INFORMAZIONI SUL SEGNALATORE

24. QUALIFICA
☐ MEDICO DI MEDICINA GENERALE ☐ FARMACISTA
☐ MEDICO OSPEDALIERO ☐ ALTRO
☐ SPECIALISTA

25. DATI DEL SEGNALATORE
NOME E COGNOME
INDIRIZZO
TEL. FAX
E-MAIL

26. DATA DI COMPILAZIONE

27. FIRMA

Inviare la scheda compilata al fax n. 06 49904248

Regione Abruzzo Dipartimento per la Salute e il Welfare