120223 Injektiolääkitykset psykiatriassa

Yl juha kemppinen

120223 Injektiolääkitykset psykiatriassa

- Agenda:

1) Psykoosilääkkeistä yleisesti
2) Injektiolääkkeistä yleisesti
3) Injektiolääkkeistä spefisesti

1. Psykoosilääkkeistä yleisesti

Yl juha kemppinen

jos hoitomyönteisyys epäilyttää missään vaiheessa, arvioi hoitomyönteisyyteen vaikuttavat tekijät, sulje pois pseudo-resistenssi, harkitse plasmapitoisuuden mittaamisen ja injektiolääkityksen tarve

kirjaa lääkevaihtoon johtaneet syyt sairauskertomukseen

harkitse jo aiemmin klotsapiinin aloitusta jos potilaalla itsetuhoisuutta, väkivaltaisuutta tai komorbidi päihdehäiriö

arvioi lääkeresinttiys uudelleen: varmista diagnoosi, tunnista mahdollinen päihdehäiriö, arvioi hoitomyönteisyys ja mahdolliset psykososiaaliset stressitekijät

huomioi kaikissa hoidon vaiheissa myös psykososiaaliset hoidot, mahdollinen kognitiivinen terapia, ammatillinen kuntoutus ja kognitiivinen kuntoutus, sekä perheen huomioiminen

- vasteen (response) systemaattinen arvioiminen oiremittareita hyödyntäen (esimerkiksi PANSS, BPRS)
- vaste on usein määritelty esimerkiksi 20 tai 30% alenemaksi oirepistemäärässä lähtötilanteeseen verrattuna

vaihe 1: ensipsykoosi
toisen polven psykoosilääke (SGA)

↓ osittainen vaste tai ei vastetta lainkaan*

vaihe 2:
jokin toinen SGA

↓ osittainen vaste tai ei vastetta lainkaan

vaihe 3:
klotsapiini

↓ osittainen vaste tai ei vastetta lainkaan

vaihe 4:
klotsapiini + (ensimmäisen polven psykoosilääke (FGA), SGA, mielialan tasaaja tai ECT)

↓ ei vastetta lainkaan

vaihe 5:
monoterapiana FGA tai S
(joita ei ole kokeiltu vaiheessa 1 tai 2)

↓ ei vastetta lainkaan

vaihe 6:
esim. SGA+FGA, SGA+SGA, (FGA tai SGA) + (ECT tai rTMS tai tDCS), (FGA tai SGA) + muu lääke, esim mielialantasaaja (esim. lamotrigiini tai topiramaatti)

lyhenteet: Brief Psychiatric Rating Scale, ECT = electroconvuisive therapy, FGA = first generation antipsychotic, PANSS = positive and negative syndrome scale, rTMS = repetitive transcranial magnetic stimulation, SGA = second generation antipsychotic, tDCS = transcranial direct current stimulation

Suvisaari J ym, Psykiatria , 2023

Maudsley Advanced Prescribing in Psychosis, 2021

Table 8.1 Outcome rating scales.

Scale	Domain	Characteristics	Download
CGI, *Clinical Global Impression*	A global rating of severity and response to treatment.	Extensive use in research Quick & easy to use Three items: severity, global improvement and efficacy	www.psywellness.com.sg/docs/CGI.pdf
GAF, *Global assessment of functioning scale*	A global rating of psychological, occupational and social functioning.	Extensive use in research Quick & easy to use One item	https://msu.edu/course/sw/840/stocks/pack/axisv.pdf
PANSS, *Positive & negative syndrome scale*	The symptoms and signs of schizophrenia.	Extensive use in research Seven positive items Seven negative items 16 general items Rating of positive items is quick and easy	http://www.emotionalwellbeing.southcentral.nhs.uk/resources/doc_download/62-panss-positive-and-negative-syndrome-scale-pdf-document
GASS, *Glasgow antipsychotic side-effect scale*	Rates the common side effects of antipsychotics.	Quick & easy to use. Patient completed questionnaire 20 items	https://mentalhealthpartnerships.com/resource/glasgow-antipsychotic-side-effect-scale/

Ehdotus skitsofrenian remissiovaiheen määritelmäksi*

*Andreasen N.C. et al. Remission in Schizophrenia: Proposed Criteria and Rationale for Consensus. Am J Psychiatry 2005; 162:441-449

Pisteluku kolme (lievä) tai vähemmän jokaisesta kahdeksasta PANSSin oireosiosta vähintään viimeisen 6 kuukauden ajalta

P1	Harhaluulot
P2	Ajatus- ja puheenhäiriöt
P3	Aistiharhat
N1	Tunneilmaisun latistuminen
N4	Sosiaalinen vetäytyneisyys
N6	Spontaanisuuden ja sujuvan keskustelun puute
G5	Luonnottomat liikkeet ja asennot
G9	Epätavalliset ja oudot ajatukset

“ Työryhmä päätyi määrittelemään remission tilaksi, jossa sairauden keskeiset oireet ovat niin lieviä, etteivät ne enää merkittävästi vaikuta potilaan käyttäytymiseen.”

Ehdotus skitsofrenian remissiovaiheen määritelmäksi*

*Andreasen N.C. et al. Remission in Schizophrenia: Proposed Criteria and Rationale for Consensus. Am J Psychiatry 2005; 162:441-449

Pisteluku kolme (lievä) tai vähemmän jokaisesta kahdeksasta PANSSin oireosiosta vähintään viimeisen 6 kuukauden ajalta

- P1 Harhaluulot
- P2 Ajatus- ja puheenhäiriöt
- P3 Aistiharhat
- N1 Tunneilmaisun latistuminen
- N4 Sosiaalinen vetäytyneisyys
- N6 Spontaanisuuden ja sujuvan keskustelun puute
- G5 Luonnottomat liikkeet ja asennot
- G9 Epätavalliset ja oudot ajatukset

“ Työryhmä päätyi määrittelemään remission tilaksi, jossa sairauden keskeiset oireet ovat niin lieviä, etteivät ne enää merkittävästi vaikuta potilaan käyttäytymiseen.”

PANSSin pistearviointi – arviointiohje

1: Puuttuu
2: Vähäinen
3: Lievä

Harhaluulot: Yksi tai kaksi harhaluuloa, jotka ovat epämääräisiä, selkiintymättömiä, eikä niistä itsepintaisesti pidetä kiinni. Harhaluulot eivät häiritse ajattelua, sosiaalisia suhteita tai käyttäytymistä.

Ajatus- ja puheenhäiriöt: Ajattelu on yksityiskohtiin takertuvaa, syrjähtelevää tai epäloogista. Ajatusten suuntaaminen päämäärään on jonkin verran vaikeaa ja stressin alaisena voi esiintyä assosiaatioiden löyhtymistä.

Aistiharhat: Yksi tai kaksi selvää mutta harvoin esiintyvää aistiharhaa, tai muutoin joukko heikkoja poikkeavia aistimuksia, jotka eivät johda ajatuksen tai käyttäytymisen vääristymiin.

Tunneilmaisun latistuminen: Kasvonilmeiden ja eleiden vaihtelut näyttävät väkinäisiltä, pakonomaisilta, keinotekoisilta tai vaihtelu puuttuu.

Sosiaalinen vetäytyneisyys: Osoittaa satunnaisesti kiinnostusta sosiaalisiin toimintoihin, mutta aloitekyky on heikko. Tavallisesti on tekemisissä toisten kanssa vain toisten aloitteesta.

Spontaanisuuden ja sujuvan keskustelun puute: Keskustelussa on vain vähän aloitteellisuutta. Potilaan vastaukset jäävät lyhyiksi ja suorasukaisiksi, haastattelijan on esitettävä suoria johdattelevia kysymyksiä.

Luonnottomat liikkeet ja asennot: Liikkeessä lievää kömpelyyttä tai asennoissa lievää jäykkyyttä.

Epätavalliset ja oudot ajatukset: Ajatussisältö on jonkin verran kummallinen tai omituinen, tai tavanomaisia ajatuksia esitetään oudossa asiayhteydessä.

4: Kohtalainen

Harhaluulot: Joko vaihteleva määrä heikosti muodostuneita, epävakaita harhaluuloja tai muutama selkeä harhaluulo, joka ajoittain häiritsee ajattelua, sosiaalisia suhteita ja käyttäytymistä.

Ajatus- ja puheenhäiriöt: Lyhyessä ja jäsennellyssä kommunikaatiossa kykenee pitämään ajatukset kasassa, mutta kommunikaation monimutkaistuessa tai vähäisenkin paineen alaisena ajatukset löyhtyvät ja muuttuvat asiaankuulumattomiksi.

Aistiharhat: Harhoja esiintyy usein mutta ei jatkuvasti, ja ne vaikuttavat potilaan ajatteluun ja käyttäytymiseen vain vähän.

Tunneilmaisun latistuminen: Kasvojen ilmeiden ja eleiden vähyys luovat raskasmielisen vaikutuksen.

Sosiaalinen vetäytyneisyys: Osallistuu passiivisesti useimpiin sosiaalisiin toimintoihin, mutta vailla mielenkiintoa ja mekaanisesti. Pyrkii vetäytymään taka-alalle.

Spontaanisuuden ja sujuvan keskustelun puute: Keskustelu ei suju vapaasti, on ontuva ja epätasainen. Johdattelevia kysymyksiä tarvitaan usein riittävän täydellisten vastausten saamiseksi ja keskustelun ylläpitämiseksi.

Luonnottomat liikkeet ja asennot: Liikkeet ovat selvästi kömpelöitä tai epäyhtenäisiä, tai asento pysyy luonnottomana lyhyitä aikoja.

Epätavalliset ja oudot ajatukset: Ajatukset ovat usein vääristyneitä ja ajoittain vaikuttavat melko eriskummallisilta.

SR Kay Positive and Negative Syndromes in Schizophrenia. Brunner Mazel 1991

Skitsofrenian remissiovaiheen arviointilomake

Mini-PANSS

Potilas: _____

Päivämäärä: _____

	Arviointi ≤ 3 tai > 3	Arviointi
P1	Harhaluulot	_____
P2	Ajatus- ja puheenhäiriöt	_____
P3	Aistiharhat	_____
N1	Tunneilmaisun latistuminen	_____
N4	Sosiaalinen vetäytyneisyys	_____
N6	Spontaanisuuden ja sujuvan keskustelun puute	_____
G5	Luonnottomat liikkeet ja asennot	_____
G9	Epätavalliset ja oudot ajatukset	_____

P1 Harhaluulot

1.1. Deluusiot. Perusteettomia, epätodellisia ja poikkeavia uskomuksia.

Luokitteluperusta: haastattelun aikana esitetty ajatussisältö ja sen vaikutus sosiaalisiin suhteisiin ja käyttäytymiseen.

1 Puuttuu - Määritelmä ei ole sovellettavissa.

2 Vähäinen - Kyseenalainen patologia; saattaa olla normaalin rajoissa.

3 Lievä - Yksi tai kaksi heikkoa, kristallisoitumatonta deluusiota, jotka eivät ole itsepintaisia. Deluusiot eivät häiritse ajattelua, sosiaalisia suhteita tai käyttäytymistä.

4 Kohtalainen - Joko kaleidoskooppinen joukko heikkoja, epävakaita deluusioita tai muutama deluusio jotka ajoittain häiritsevät ajattelua, sosiaalisia suhteita tai käyttäytymistä.

5 Kohtalaisen vaikea - Lukuisia selviä, itsepintaisia deluusioita, jotka ajoittain häiritsevät ajattelua, sosiaalisia suhteita tai käyttäytymistä.

6 Vaikea - Vakiintuneita deluusioita, jotka ovat kristallisoituneita, mahdollisesti systematisoituneita, itsepintaisia ja häiritsevät selvästi ajattelua, sosiaalisia suhteita tai käyttäytymistä.

7 Erittäin vaikea - Vakiintuneita deluusioita, jotka ovat joko erittäin systematisoituneita tai lukuisia ja jotka hallitsevat potilaan elämää monitahoisesti. Seurauksena on usein sopimaton ja vastuuton toiminta, joka voi jopa vaarantaa potilaan tai muiden turvallisuuden.

P2 Ajatus- ja puheenhäiriöt

1.2. Hajanainen käsityskyky. Hajanainen ajatteluprosessi, jota luonnehtii häiriintynyt päämäärähakuinen päättely, esim. seikkaperäisyys, sekundäärisyys, löyhät assosiaatiot, epäjohdonmukaisuus, karkea epäloogisuus tai ajatuskatko.

Luokitteluperusta: kognitiivisverbaalisten prosessien havainnointi haastattelun aikana.

1 Puuttuu - Määritelmä ei ole sovellettavissa.

2 Vähäinen - Kyseenalainen patologia, saattaa olla normaalin rajoissa.

3 Lievä - Ajattelu on seikkaperäistä, sekundääristä tai paraloogista. Ajatusten suuntaaminen päämäärään on jonkin verran vaikeaa ja stressin alaisena voi esiintyä assosiaatioiden löyhtymistä.

4 Kohtalainen - Lyhyessä ja jäsennellyssä kommunikaatiossa kykenee fokusoimaan ajatukset, mutta ne löyhtyvät ja muuttuvat asiaankuulumattomiksi kun kommunikaatio on monimutkaisempaa tai kun on stressaantunut.

5 Kohtalaisen vaikea - Ajatusten järjestäminen on yleensä vaikeaa ja esiintyy paljon irrevalenttia, epäjohdonmukaista, sekä assosiaatioiden löyhtymistä myös ilman stressiä.

6 Vaikea - Ajatukset ovat vaikeasti pois raiteiltaan ja sisäisesti epäjohdonmukaisia, minkä vuoksi esiintyy lähes jatkuvasti paljon asiaankuulumatonta sekä ajatusprosessien häiriintymistä.

7 Erittäin vaikea - Ajatukset ovat häiriintyneet niin että potilas on inkoherentti. Assosiaatioiden löyhtyminen on huomattava ja seurauksena on täydellinen kommunikaatiokyvyttömyys, kuten "sanasalaatti!" tai mutismi.

P3 Aistiharhat

1.3. Harhainen käytös. Verbaalinen ilmaus tai käyttäytyminen ilmaisee aistimuksia, joita eivät saa aikaan ulkoiset ärsykkeet. Niitä voi olla kuulo-, näkö-, haju- tai tuntoaistin alueella.

Luokitteluperusta: sanallinen tai fyysinen ilmaus haastattelun aikana sekä perusterveydenhuollon tai perheen tiedot käyttäytymisestä.

1 Puuttuu - Määritelmä ei ole sovellettavissa.

2 Vähäinen - Kyseenalainen patologia; saattaa olla normaalin rajoissa.

3 Lievä - Yksi tai kaksi selvää harvoin esiintyvää aistiharhaa, tai muutoin joukko heikkoja poikkeavia aistimuksia jotka eivät johda ajatuksen tai käyttäytymisen vääristymiin.

4 Kohtalainen - Harhoja esiintyy usein mutta ei jatkuvasti, ja ne vaikuttavat potilaan ajatteluun ja käyttäytymiseen vain vähän.

5 Kohtalaisen vaikea - Harhat ovat toistuvia, ne voivat esiintyä useamman kuin yhden aistin alueella ja ne pyrkivät vääristämään ajattelua ja/tai häiritsemään käyttäytymistä. Potilas voi tulkita näitä kokemuksia delusionaalisesti ja vastata niihin emotionaalisesti sekä toisinaan myös verbaalisesti.

6 Vaikea - Harhoja esiintyy lähes jatkuvasti ja ne häiritsevät huomattavasti ajattelua ja käyttäytymistä. Potilas pitää niitä todellisina aistimuksina ja monet emotionaaliset ja verbaaliset vastineet harha-aistimuksiin estävät toimintaa.

7 Erittäin vaikea - Potilas on lähes täysin harhojensa vallassa. Harhat käytännöllisesti katsoen hallitsevat ajattelua ja käytöstä. Harha-aistimusten tulkinta on rigidin delusionaalista ja niihin vastataan verbaalisesti ja käyttäytymisellä. Potilas noudattaa käskeviä harha-aistimuksia.

N1 Tunneilmaisujen latistuminen

2.1. Tunteettomuus. Vähentynyt emotionaalinen herkkyys, jota luonnehtivat alentunut kasvojen ilmeikkyys, tunteiden vaihtelu ja kommunikaatioeleet.

Luokitteluperusta: haastattelun aikaiset havainnot mielialan ja emotionaalisen herkkyyden fyysisistä ilmentymistä.

1 Puuttuu - Määritelmä ei ole sovellettavissa.
2 Vähäinen - Kyseenalainen patologia; saattaa olla normaalin rajoissa.
3 Lievä - Kasvojen ilmeiden ja kommunikaatioeleiden muutokset näyttävät väkinäisiltä, pakonomaisilta, keinotekoisilta tai vaihtelu puuttuu.
4 Kohtalainen - Kasvojen ilmeiden vähyyden ja vähäisten eleiden vuoksi olemus on tylsä.
5 Kohtalaisen vaikea - Tunteet yleensä "latteita"; kasvojen ilmeet vaihtelevat vain satunnaisesti ja kommunikaatioeleet ovat harvalukuisia.
6 Vaikea - Suurimman osan ajasta huomattavaa tunteiden latteutta ja vajavuutta. Saattaa esiintyä moduloimattomia ääritunteenpurkauksia kuten kiihtymystä, raivoa ja epäasiallista, konrolloimatonta naurua.
7 Erittäin vaikea - Kasvojen ilmeet ja kommunikaatioeleet puuttuvat käytännöllisesti katsoen kokonaan. Potilas vaikuttaa kuivakkaalta ja puisevalta.

N4 Sosiaalinen vetäytyneisyys

2.4. Passiivinen/apaattinen sosiaalinen vetäytyminen. Mielenkiinto ja aloitekyky sosiaaliseen kanssakäymiseen on vähentynyt passiivisuuden, apatian, voimattomuuden tai tahdonvoiman puutteen vuoksi. Seurauksena on alentunut vuorovaikutus ja päivittäisen elämäntoimintojen laiminlyönti.

Luokitteluperusta: perusterveydenhuollon ja perheen tiedot sosiaalisesta käyttäytymisestä.

1 Puuttuu - Määritelmä ei ole sovellettavissa.
2 Vähäinen - Kyseenalainen patologia; saattaa olla normaalin rajoissa.
3 Lievä - Osoittaa satunnaisesti mielenkiintoa sosiaalisiin aktiviteetteihin, mutta aloitekyky on heikko. Tavallisesti on tekemisissä toisten kanssa vain toisten aloitteesta.
4 Kohtalainen - Osallistuu passiivisesti useimpiin sosiaalisiin aktiviteetteihin, mutta vailla mielenkiintoa ja mekaanisesti. Pyrkii vetäytymään taka-alalle.
5 Kohtalaisen vaikea - Osallistuu passiivisesti vain vähäisiin toimintoihin eikä käytännöllisesti katsoen osoita mielenkiintoa eikä aloitteellisuutta. Viettää yleensä vähän aikaa toisten kanssa.
6 Vaikea - On apaattinen ja eristäytyy, osallistuu perin harvoin sosiaalisiin aktiviteetteihin ja ajoittain lyö laimin henkilökohtaiset tarpeensa. Spontaaneja sosiaalisia kontakteja on erittäin vähän.
7 Erittäin vaikea - Perin pohjin apaattinen, sosiaalisesti eristäytynyt ja laiminlyö itsensä.

N6 Spontaanisuuden ja sujuvan keskustelun puute

2.6. Spontaanisuuden puute ja keskustelun kulku. Normaalin kommunikaation alentuminen apatiaan, tahdonvoiman puutteeseen, defensiivisyyteen tai kognitiiviseen vajavuuteen liittyen. Ilmenee verbaalis-vuorovaikutuksellisen prosessin joustavuuden ja tuottavuuden vähenemisenä.

Luokitteluperusta: kognitiivis-verbaalisten prosessien havainnointi haastattelun aikana.

1 Puuttuu - Määritelmä ei ole sovellettavissa.
2 Vähäinen - Kyseenalainen patologia; saattaa olla normaalin rajoissa.
3 Lievä - Keskustelussa vähän aloitteellisuutta. Potilaan vastaukset jäävät lyhyiksi ja kaunistelemattomiksi; ne vaativat haastattelijan suoria ja johdattelevia kysymyksiä.
4 Kohtalainen - Keskustelu ei kulje vapaasti, vaan tuntuu epätasaiselta ja ontuvalta. Tarvitaan usein johdattelevia kysymyksiä nostattamaan adekvaatteja vastauksia ja edistämään keskustelua.
5 Kohtalaisen vaikea - Potilas osoittaa huomattavan spontaanisuuden ja avoimmuuden puutetta ja vastaa haastattelijan kysymyksiin vain yhdellä tai kahdella lyhyellä lauseella.
6 Vaikea - Potilaan vastaukset rajoittuvat etupäässä muutamaan sanaan tai lyhyeen lauseeseen tarkoituksena välttää tai lyhentää kommunikaatiota. (Esim. "En tiedä", "En pysty sanomaan.") Sen seurauksena keskustelu on erittäin vaikeaa eikä haastattelu tuota tulosta.
7 Erittäin vaikea - Verbaalinen ilmaisu rajoittuu pelkästään satunnaiseen äännähdykseen; keskustelu on mahdotonta.

G5 Luonnottomat liikkeet ja asennot

3.5. Maneerit ja asennot. Luonnoton liikehdintä tai asento, jota luonnehtii kömpelö, väkinäinen, hajanainen tai bisarri olemus.

Luokitteluperusta: fyysisten manifestaatioiden havainnointi haastattelun aikana sekä perusterveydenhuollon ja perheen tiedot.

1 Puuttuu - Määritelmä ei ole sovellettavissa.

2 Vähäinen - Kyseenalainen patologia; saattaa olla normaalin rajoissa.

3 Lievä - Liikkeissä lievää kömpelyyttä tai asennossa lievää jäykkyyttä.

4 Kohtalainen - Liikkeet ovat selvästi kömpelöitä tai hajanaisia, tai asento pysyy luonnottomana lyhyitä aikoja.

5 Kohtalaisen vaikea - Havaittavissa satunnaisia bisarreja rituaaleja tai luonnoton asento säilyy pitkiä aikoja.

6 Vaikea - Bisarreja rituaaleja toistetaan usein, maneereita, stereotyyppistä liikehdintää, vääristynyt asento pysyy pitkiä aikoja.

7 Erittäin vaikea - Toimintaa häiritsee vaikea, käytännössä jatkuva rituaalien, maneerien tai stereotyyppisen liikehdinnän noudattaminen tai pysyvä luonnoton asento joka säilyy suurimman osan aikaa.

G9 Epätavalliset ja oudot asennot

3.9. Epätavallinen ajatussisältö. Ajattelua luonnehtivat oudot, mielikuvitukselliset ja bisarrit ajatukset, jotka vaihtelevat etäisistä ja epätyypillisistä vääristyneisiin, epäloogisiin ja avoimen absurdeihin.

Luokitteluperusta: haastattelun aikana ilmaistu ajatussisältö.

1 Puuttuu - Määritelmä ei ole sovellettavissa.
2 Vähäinen - Kyseenalainen patologia; saattaa olla normaalin rajoissa.
3 Lievä - Ajatussisältö on jonkin verran omituinen tai poikkeava, tai tuttujen ajatusten sisältö outo.
4 Kohtalainen - Ajatukset ovat usein vääristyneitä ja ajoittain vaikuttavat melko bisarreilta.
5 Kohtalaisen vaikea - Potilas esittää monia outoja ja mielikuvituksellisia ajatuksia (esim. että on kuninkaan adoptiopoika, että on paennut kuolleista) tai avoimen absurdeja ajatuksia (esim. että potilaalla on satoja lapsia, että saa hammaspaikan välityksellä radiolähetyksiä ulkoavaruudesta).
6 Vaikea - Potilas osoittaa monia epäloogisia ja absurdeja ajatuksia tai ajatuksia joiden sisältö on selvän bisarri (esim. että potilaalla on kolme päätä, että on vieras toiselta planeetalta).
7 Erittäin vaikea - Ajattelu on täynnä absurdeja, bisarreja ja groteskeja ajatuksia.

The metabolic syndrome

Measure	Value
Waist circumference	male ≥94 cm, 37 in.; female ≥80 cm, 31.5 in.
High density lipoprotein (HDL)	male <1.03 mmol l^{-1}; female <1.29 mmol l^{-1}
Triglycerides	≥1.7 mmol l^{-1}
Glucose dysregulation	>5.5 mmol l^{-1} (*fasting blood glucose*)
Blood pressure	≥130/85 mmHg

Waist criteria + 2 others = metabolic syndrome.

Physical health monitoring for patients prescribed antipsychotics

Measure	At baseline	Initiation phase	At 3 month stage	Every 6 months	Annually
Weight	×	Weekly for 6 weeks		×	
Nutrition risk screening at baseline. Advice & information on cardioprotective diet at NHS Choices: http://www.nhs.uk/Livewell/healthy-eating/Pages/Healthyeating.aspx Referral to dietitian? Exercise. Physical activity guidelines for adults at NHS Choices: http://www.nhs.uk/Livewell/fitness/Pages/physical-activity-guidelines-for-adults.aspx					
Waist circumference	×		×		×
Smoking status	×				×
Nicotine replacement therapy should be considered as first-line pharmacotherapy. There are multiple preparations, and all routes of administration are effective at ameliorating symptoms of withdrawal and are associated with improved rates of smoking cessation. Dosages will vary according to the degree of nicotine dependence. Simultaneous use of long- (e.g. patch) and intermittent short-acting formulations (e.g. spray) appear to be more effective, and duration of treatment can last 8–12 weeks [385]. second-line: varenicline, bupropion.					
Diabetes screening ▪ Fasting blood glucose ▪ Hb1Ac	×	Monthly for 3 months on clozapine or olanzapine	×		×
Lipids	×		×		×
Blood pressure/pulse	×		×		×
Temperature	×		×		×
Full physical examination	×				×

(Continued)

74 Advanced Prescribing in Psychosis

Measure	At baseline	Initiation phase	At 3 month stage	Every 6 months	Annually
Extra-pyramidal signs, especially if: ■ high-potency D_2 drug.	x	Weekly for 6 weeks	x		
ECG if: ■ Inpatients ■ Personal or family history of CVS disease. ■ Risk factors for long QTc. ■ Hypertension. ■ Haloperidol, clozapine.	x				x
U&E's, FBC, LFTs	x				x
CK, prolactin	x				

050923 Psyykenlääkkeet (uudet) jolla on antipsykoottista vaikutusta

- Pitoisuusmittaukset
- Jäännöspitoisuuden mittaaminen
- Kun mitataan lääkeaineiden seerumipitoisuuksia, **näytteenotto ajoitetaan niin sanotun jäännöspitoisuuden ajankohtaan, joka on aamulla ennen aamulääkkeen ottoa**. Viitearvot ovat jäännöspitoisuuksia.
- Kun lääkkeen annostelua muutetaan, muutoksen jälkeinen pitoisuuden vakaa tila saavutetaan noin **5 puoliintumisajan** jälkeen.
- Siten esimerkiksi, jos **litiumin** (T½ 14–30 tuntia) annoksen noston jälkeen halutaan selvittää, minkä pitoisuuden uusi annos tuottaa, tulisi näyte ottaa vasta noin 1 viikon kuluttua annosmuutoksesta. **Tosin lähes 90 % pitoisuuden kasvusta tapahtuu jo 3 puoliintumisajan aikana**.
- Keskeiset mitattavat lääkeaineet
- Litiumin tai trisyklisten masennuslääkkeiden käyttö edellyttää **aina** seerumipitoisuuksien mittaamista tehokkaan ja turvallisen lääkeannoksen määrittämiseksi. Pitoisuusmittauksia tulee hyödyntää myös käytettäessä valproaattia tai karbamatsepiinia.
- Klotsapiinin kohdalla niiden käyttö on myös vahvasti suositeltavaa.
- Lähes kaikkien muiden psyykenlääkkeiden kohdalla pitoisuusmittauksista voi olla hyötyä tietyissä ongelmatilanteissa.

2021 Meyer and Stahl The clinical use of antipsychotic plasma levels

Box 1.1 Why Five Half-Lives Equates to Steady State

Example: Antipsychotic with a 24-hour half-life is dosed once daily. The accumulated medication levels and contribution from each dose are noted below. After five half-lives, the medication is at 97% of the steady state value.

	1st dose	2nd dose	3rd dose	4th dose	5th dose	Total
24 hours	50%	–	–	–	–	50%
48 hours	25%	50%	–	–	–	75%
72 hours	12.5%	25%	50%	–	–	87.5%
96 hours	6.25%	12.5%	25%	50%	–	93.75%
120 hours	3.125%	6.25%	12.5%	25%	50%	96.875%

Meyer and Stahl, 2021

050923 Psyykenlääkkeet (uudet) jolla on antipsykoottista vaikutusta

Taulukko 1. Eräiden psykoosilääkkeiden **95 % tehosta tuottava vuorokausiannos (ED95%)** ja siitä laskettu ekvivalenttiannos, joka vastaa 1 mg:n suun kautta otetun risperidonin tehoa.

[1] ED95% (keskiluku) on vuorokausiannos (*per os*), jolla saavutetaan 95 % lääkkeen antipsykoottisesta tehosta.
[2] Lääkeannos, joka vastaa suun kautta annosteltavan 1 mg risperidoniannoksen antipsykoottista tehoa.

Lääke	ED95%[1]	Ekvivalenttiannos[2] (vastaa **1 mg risperidonia per os)**
Amisulpridi	537,0 mg	85,8 mg
Aripipratsoli	11,5 mg	1,8 mg
Asenapiini	15,0 mg	2,4 mg
Brekspipratsoli	3,36 mg	**0,54** mg
Haloperidoli	6,3 mg	1,01 mg
Ketiapiini	482,0 mg	77,0 mg
Lurasidoni	147,0 mg	**23,5** mg
Olantsapiini	15,2 mg	2,4 mg
Paliperidoni	13,4 mg	2,1 mg
Risperidoni	6,3 mg	1,0 mg
Sertindoli	22,5 mg	3,6 mg
Tsiprasidoni	186,0 mg	30,0 mg

Timo Partonen, Kari Raaska, Olli Kampman ja Jouko Lönnqvist, Psykiatria 2021

2021 Meyer and Stahl The clinical use of antipsychotic plasma levels

Table P3 Mean half-life of commonly used oral antipsychotics and important metabolites [8–18, 3, 19, 20]

Drug	$T_{1/2}$ (hours)	5 x T1/2
First-generation antipsychotics		
Chlorpromazine	11.05–15	75 tuntia
Fluphenazine	13	65 tuntia
Haloperidol	24	120 tuntia
Loxapine	4	20 tuntia
7-OH loxapine	??[a]	
Molindone	2[b]	10 tuntia

Meyer and Stahl, 2021

2021 Meyer and Stahl The clinical use of antipsychotic plasma levels

Drug		$T_{1/2}$ (hours)	
Perphenazine	**Peratsin**	9–12	60 tuntia
Zuclopenthixol	**Cisordinol**	17.6	88 tuntia
Newer antipsychotics			
Amisulpride	**Solian**	12	
Aripiprazole	**Abilify**	75	375 tuntia
Asenapine sublingual Asenapine transdermal patch	**Sycrest**	24 30[c]	150 tuntia
Brexpiprazole	**Rxulti**	91	455 tuntia
Cariprazine Desmethylcariprazine (DCAR) Didesmethylcariprazine (DDCAR)	**Reagila**	31.6–68.4 29.7–39.5 (DCAR) 314–446 (DDCAR)	342 tuntia
Clozapine Norclozapine	**Leponex**	9–17 20	100 tuntia
Iloperidone	**Fanaptum**	15–22	110 tuntia
Lumateperone	**Caplypta**	18	90 tuntia
Lurasidone	**Latuda**	28.8–37.4[d]	187 tuntia
Olanzapine	**Zyprexa**	30	150 tuntia
Paliperidone (9-OH risperidone)[e]	**Xeplion**	23	115 tuntia
Quetiapine Norquetiapine	**Ketipinor**	7 12	60 tuntia
Risperidone Paliperidone (9-OH risperidone)[f]	**Risperdal**	3 21	105 tuntia
Sertindole	**Serdolect**	60–73	365 tuntia
Ziprasidone	**Ziprasidon**	7	35 tuntia

Meyer and Stahl, 2021

2. Psykoosilääkkeistä erityisesti

Yl juha kemppinen

2020 Puzantian et al

LONG-ACTING INJECTABLE (LAI) Antipsychotics

INTRODUCTION: DO LAIs WORK?

These formulations used to be known as "depot" antipsychotics, but the powers that be have renamed them "long-acting injectables" (LAIs), presumably to help remove some of the stigma associated with their use.

The potential advantages of LAIs are numerous, and include the following:

- LAIs ensure that otherwise non-adherent patients have robust serum levels of antipsy
- Serum levels are more consistent over time than they are with oral meds
- Both families and clinicians spend less time struggling with patients about medication adherence
- LAIs present a lower risk of overdose because you aren't providing your patient with large quantities of pills

- Parempi seerumitaso
- Seerumitaso on tasaisempi kuin PO
- Lääkesitoutumista ei tarvitse pohtia
- Ei yliannostusriskiä

Studies attempting to demonstrate advantages of LAIs have been mixed. One large meta-analysis found no difference between LAIs and oral meds in relapse rates, with the exception of first-generation LAIs in older studies (Kishimoto T et al, *Schiz Bull* 2014;40(1):192–213). But a meta-analysis of 25 naturalistic observational studies, involving 5,940 patients, found that switching these patients to LAIs strongly decreased the number of hospitalizations (Kishimoto T et al, *J Clin Psychiatry* 2013;74(10):957–965).

The bottom line is that patients who do poorly on pills because of non-adherence are likely to do better on LAIs—if you can get them to agree to getting an injection.

DECIDING AMONG THE LAIs

Kärsivällisyys : injektion terapeuttinen taso vie enemmän aikaa

2020 Puzantian et al

DECIDING AMONG THE LAIs

General Notes on LAIs

- It's best to choose an LAI version of an oral medication that your patient has already taken, so that you can be more confident that the agent is effective and tolerable.
- Be patient. The full therapeutic effect of LAIs can take longer than orals—ie, several months. Don't adjust the LAI dose prematurely.
- Consider oral overlap. Agents differ on how quickly you can titrate up the dose. This is important because for those requiring gradual titration, patients will need oral pills to make sure they have a decent serum level right away. This process is called the "oral overlap" and it has two disadvantages. First, it makes the process of dosing a bit more complex (not a huge deal); second, if the patient is refusing to take oral meds (but accepting an injection, either under court order or voluntarily), you'll have to choose a different LAI or risk a decompensation while waiting for levels to become therapeutic.
- *Never* initiate an LAI on a patient who has a history of neuroleptic malignant syndrome (NMS) on any antipsychotic. That's just asking for trouble.

Injektio ei MNS:n kokeneelle

LAI Options

- There's a pretty comprehensive table on the following pages that reports, for each LAI, the **FDA indication(s), medication names, costs, available strengths, dosing information,** and **pharmacokinetics** (need for oral overlap and dosing interval). But here, we'll give you a shorthand version of the most relevant **clinical pearls** below:

Typical antipsychotics

Siqualone

- **Fluphenazine (Prolixin Decanoate)**—Dosed every 2 weeks. Injections are painful. Cheap, but relatively high risk of EPS and TD. Oral overlap required.

Serenase

- **Haloperidol (Haldol Decanoate)**—Dosed monthly. As cheap as Prolixin, and since it's dosed less often and the pharmacokinetics are more predictable, it's generally the better choice among FGAs. Oral overlap required, although some use a "loading dose" method (20 times oral dose, followed by 10–15 times oral dose in subsequent months) which requires no oral overlap (Ereshefsky L et al, *Hosp Community Psychiatry* 1993;44(12):1155–1161).

Atypical antipsychotics

Abilify

- **Aripiprazole (Abilify Maintena)**—Dosed monthly. Oral overlap required for 14 days. Deltoid or gluteal injection. Expensive. Good side effect profile.
- **Aripiprazole lauroxil (Aristada)**—This prodrug of aripiprazole is dosed monthly, every 6 weeks, or every 2 months. Smallest dose (441 mg monthly) may be given deltoid or gluteal; other doses must be given gluteal. Dosing interval

2020 Puzantian et al

flexibility makes this formulation appealing, although oral overlap is required for 21 days. You can forgo the oral overlap if you give your patient a dose of **Aristada Initio** 675 mg plus 30 mg oral aripiprazole on the same day as your first dose of Aristada. Expensive, but a good side effect profile.

Zypadhera

- **Olanzapine (Zyprexa Relprevv)**—Dosed either every 2 weeks or monthly, depending on the dose needed. May be the worst choice among all LAIs for multiple reasons. High potential for weight gain. There's a small risk of a post-injection delirium/sedation syndrome, occurring in less than 1% of patients, caused by accidental intravascular injection. For this reason, you have to give the injection at a registered health care facility where patients can be continuously monitored for at least 3 hours after the injection. Restricted use requires physician and facility registration, and additional paperwork with Eli Lilly's program. High cost, restriction of use, monitoring requirement, and risk of adverse outcome all limit use severely. Gluteal injection only. Expensive. No oral overlap.

Xeplion

- **Paliperidone palmitate monthly (Invega Sustenna)**—Monthly dosing. Less painful injection than Risperdal Consta or Zyprexa Relprevv. No oral overlap required; need for 2 separate loading injections makes initiation a bit more complicated. First 2 doses deltoid; subsequent doses may be deltoid or gluteal. Expensive. No oral overlap and potential to transition to every-3-month formulation are appealing features.

Trevicta

- **Paliperidone palmitate every 3 months (Invega Trinza)**—Every-3-month dosing, but your patient must have done well on monthly injections of Sustenna for at least 4 months before switching to Trinza. Deltoid or gluteal injection. Must shake syringe vigorously for at least 15 seconds to ensure uniform suspension of long-acting particles and prevent clogging in needle. Expensive. No oral overlap.

Risperdal Consta

- **Risperidone (Risperdal Consta)**—Every-2-week dosing. A 3-week oral overlap and the need for a refrigerated solution make this LAI more cumbersome to use than some of its competitors. Painful injection. Must shake for at least 10 seconds to ensure uniform suspension of microspheres. Deltoid or gluteal. Expensive.

← jääkaappi

Subcuta, ei SF

- **Risperidone (Perseris)**—This a monthly option for risperidone, an improvement over the every-2-week dosing of Consta. Another advantage is that no oral overlap is required. It's also the first LAI to be dosed subcutaneously (into the abdomen) rather than a deep and more painful IM injection. Note that the highest dose of Perseris is equivalent to 4 mg/day of oral risperidone, so this isn't a good option for patients on higher doses. Expensive.

Antipsycho

General Notes on Administration of LAIs

- Most LAI are administered by deep IM injection (the exception is risperidone Perseris, which is administered subcutaneously). To ensure medication is delivered effectively into deep muscle and not subcutaneous fatty tissue (which would delay absorption significantly), administer to the ventrogluteal muscle (of the hip). This muscle is easily located and relatively free of major blood vessels and nerves.
- Z-track technique should be used when administering fluphenazine or haloperidol decanoate to gluteal muscle. To do this, stretch and displace the skin by pulling it laterally away from the intended point of injection. Insert the needle into the site at a 90-degree angle; aspirate by pulling back on the plunger for 5 seconds, allowing time for any blood to travel from a penetrated vessel up the bore of the needle. If blood is aspirated, withdraw the needle and seal the wound; repeat at another site with new needle. If no blood is aspirated, give the injection, wait 10 seconds, and then withdraw the needle and release the skin, allowing the displaced tissue to seal the needle track. You can use the Z-track technique with other agents also to ensure deep IM administration and minimize or prevent drug leakage.
- In general, women tend to have more fatty tissue in the gluteal area, especially in the dorsogluteal muscle, and this should be considered when choosing needle length. Longer needles should also be used in obese patients. When medication is delivered into fatty tissue inadvertently, the patient is at increased risk for granuloma, sterile abscess, redness and swelling, ulceration, or fat necrosis.
- Maximum recommended volume to be administered:
  - Gluteal: 3 mL
  - Deltoid: 2 mL
- Aspiration to ensure needle tip has not accidentally punctured a blood vessel is generally good practice. However, it is not possible with pre-filled syringe formulations of Abilify Maintena, Aristada, or Aristada Initio due to the syringe design.
- Administer dose immediately after suspending and/or shaking to avoid settling or needle occlusion. See product information for specific details on preparation and administration.
- **Do not massage the injection site** (and advise patients not to massage the site) because this can promote dispersal into fatty tissue.

Table 1.4 Antipsychotic long-acting injections – doses and frequencies[15]

Drug	UK Trade Name	Licences injection site	Test dose (mg)	Dose range (mg/week)	Dosing interval (weeks)	Comments
Aripiprazole	(Abilify Maintena)	Buttock	Not required**	300–400mg monthly	Monthly	Does not increase prolactin; oral loading required
Flupentixol decanoate	**Fluanxol**	Buttock or thigh	20	50mg every 4 weeks to 400mg a week	2–4	Maximum licensed dose is high relative to other LAIs
Fluphenazine decanoate	(Modecate)	Gluteal region	12.5	12.5mg every 2 weeks to 100mg every 2 weeks	2–5	High EPS
Haloperidol decanoate	**Serenase**	Gluteal region	25*	50–300mg every 4 weeks	4	High EPS
Olanzapine pamoate	(ZypAdhera)	Gluteal	Not required**	150mg every 4 weeks to 300mg every 2 weeks	2–4	Risk of post-injection syndrome
Paliperidone palmitate (monthly)	(Xeplion)	Deltoid or gluteal	Not required**	50–150mg monthly	Monthly	Loading dose required at treatment initiation
Paliperidone palmitate (3-monthly)	(Trevicta)	Deltoid or gluteal	Not required***	175–525mg every 3 months	3 months	
Pipothiazine palmitate	(Piportil)	Gluteal region	25	50–200mg every 4 weeks	4	? Lower incidence of EPS (relative to other FGAs)
Risperidone microspheres	(Risperdal Consta)	Deltoid or gluteal	Not required**	25–50mg every 2 weeks	2	Drug release delayed for 2–3 weeks – oral therapy required
Zuclopenthixol decanote	**Cisordinol**	Buttock or thigh	100	200mg every 3 weeks to 600mg a week	2–4	? Slightly better efficacy than LAI FGAs

Notes:

- The doses mentioned above are for adults. Check formal labelling for appropriate doses in the elderly.
- After a test dose, wait 4–10 days then titrate to maintenance dose according to response (see product information for individual drugs).
- Avoid using shorter dose intervals than those recommended except in exceptional circumstances (e.g. long interval necessitates high volume (>3–4ml?) injection). Maximum licensed single dose overrides longer intervals and lower volumes. For example, zuclopenthixol 500mg every week is licensed, whereas 1,000mg every two weeks is not (more than the licensed maximum of 600mg is administered). Always check official manufacturer's information.

*Test dose not stated by manufacturer.

**Tolerability and response to the oral preparation should be established before administering the LAI. With respect to paliperidone LAI, oral risperidone can be used for this purpose.

***May not be started until the completion of 4 months' treatment with monthly LAI.

Depot/LAI antipsychotics – pharmacokinetics

Drug	UK Trade Name	Time to peak (days)*	Plasma half-life (days)	Time to steady state (weeks)**
Aripiprazole[1]	(Abilify Maintena)	7d	30–46d	~20W
Aripiprazole lauroxil[2–4]	(Aristada (in USA))	44–50d	~54–57d	~16W
Aripiprazole lauroxil nanocrystal[4–6]****	(Aristada Initio (in USA))	4d	~15–18d	
Flupentixol decanoate[7,8]	(Depixol)	4–7d	8–17d	~8–12W
Fluphenazine decanoate[4,9–11]	(Modecate)	8–12d***	7–10d	~8W
Haloperidol decanoate[12,13]	(Haldol)	7d	21d	~14W
Olanzapine pamoate[4,14,15]	(ZypAdhera)	2–3d	30d	~12W
Paliperidone palmitate[4,16] (monthly)	(Xeplion)	13d	25–49d	~20W
Paliperidone palmitate[17,18] (three monthly)	(Trevicta)	25d	Deltoid: 84–95d Gluteal: 118–139d	~52W
Pipotiazine palmitate[19,20]	(Piportil)	7–14d	15d	~9W
RBP-7000[4,21] (risperidone sc monthly)	(Perseris (in USA))	1st peak ~1d 2nd peak ~11d	~8–9d	~8W
Risperidone microspheres[22,23]	(Risperidal Consta)	~30d	4d	~8W
Zuclopenthixol decanoate[7,19,24]	(Clopixol)	4–7d	19d	~12W

*Time to peak is not the same as time to reach therapeutic plasma concentration, but both are dependent on dose. For large (loading) doses, therapeutic activity is often seen before attaining peak levels. For low (test) doses, the initial peak level may be sub-therapeutic.

**Attainment of steady state (SS) follows logarithmic, not linear characteristics: around 90% of SS levels are achieved in three half-lives. Time to attain steady state is independent of dose and dosing frequency (i.e. you can't hurry it up by giving more, more often). Loading doses can be used to produce prompt therapeutic plasma levels but time to SS remains the same.

***Some estimates suggest peak concentrations after only a few hours.[24,25] It is likely that fluphenazine decanoate produces two peaks – one on the day of injection and a second slightly higher peak a week or so later.[12]

****used to initiate treatment with Aristada, IM injection with one 30 mg oral dose of aripiprazole; not designed for repeat dosing.

TABLE 9: Long-Acting Injectable Antipsychotics

Generic Name (Brand Name) Year FDA Approved *[G] denotes generic availability*	Relevant FDA Indication(s)	Available Strengths	Oral Overlap	Dosing Interval	Initial Dosing	Maintenance Dose	Cost for Monthly Supply at Average Dose (July 2019)
Typical antipsychotics							
Fluphenazine decanoate [G] (Prolixin Decanoate[1]) 1972	Schizophrenia	25 mg/mL	Continue total oral dose for 2–3 days, then ↓ by 50% increments every 2–3 days until discontinued (by next injection)	2 weeks	1.25x total daily oral dose Q2–3 weeks	Increase in increments of 12.5 mg; do not exceed 100 mg per dose	$ [G]
Haloperidol decanoate [G] (Haldol Decanoate) 1986	Schizophrenia	50 mg/mL and 100 mg/mL	For 7 days, give usual oral dose, then ↓ by 50% weekly for 2 weeks, then discontinue; alternatively, no oral overlap if 20x oral loading dose given	4 weeks	10-15x total oral daily dose (or 20x if loading dose with no oral overlap) Q4 weeks. First dose should be ≤100 mg; if higher dose needed, give remainder in 1–2 weeks.	Continue 10–15x total oral daily dose Q4 weeks	$ [G] $$$$ Haldol Dec
Atypical antipsychotics							
Aripiprazole (Abilify Maintena) 2013	Schizophrenia Bipolar disorder	300 mg and 400 mg vials and pre-filled syringes	For 14 days	4 weeks	400 mg Q4 weeks	400 mg Q4 weeks; decrease to 300 mg Q4 weeks if side effects	$$$$$
Aripiprazole lauroxil (Aristada) 2015	Schizophrenia	441 mg, 662 mg, 882 mg, 1064 mg	For 21 days	Monthly, every 6 weeks, or every 2 months	441 mg, 662 mg, or 882 mg monthly (equiv to 10, 15, and 20 mg/day); or 882 mg every 6 weeks (15 mg/day); or 1064 mg every 2 months (15 mg/day)	Continue initial dosing or adjust based on clinical response	$$$$$
Aripiprazole lauroxil (Aristada Initio) 2018	Schizophrenia	675 mg syringe	Aripiprazole 30 mg PO x 1 day	See Aristada above	To be given as single initial dose, in conjunction with Aristada as above (same day)	See above	$$$$$
Olanzapine (Zyprexa Relprevv) 2009	Schizophrenia	210, 300, and 405 mg vials	No overlap	2–4 weeks	10 mg/day oral: 210 mg Q2 weeks x 4 doses or 405 mg Q4 weeks x 2 doses 15 mg/day oral: 300 mg Q2 weeks x 4 doses 20 mg/day oral: 300 mg Q2 weeks	10 mg/day oral: 150 mg Q2 weeks or 300 mg Q4 weeks 15 mg/day oral: 210 mg Q2 weeks or 405 mg Q4 weeks 20 mg/day oral: 300 mg Q2 weeks Maximum dose: 300 mg Q2 weeks or 405 mg Q4 weeks	$$$$$

[1]brand discontinued; available as generic only

Generic Name (Brand Name) Year FDA Approved *[G] denotes generic availability*	Relevant FDA Indication(s)	Available Strengths	Oral Overlap	Dosing Interval	Initial Dosing	Maintenance Dose	Cost for Monthly Supply at Average Dose (July 2019)
Paliperidone palmitate (Invega Sustenna) 2009	Schizophrenia Schizoaffective disorder (monotherapy or adjunct)	39, 78, 117, 156, and 234 mg in prefilled syringes	No overlap	4 weeks	234 mg IM in deltoid, then 156 mg 1 week later	117 mg 3 weeks after 2nd dose then Q month; may adjust monthly dose (maintenance given deltoid or gluteal) Approx. equivalence: 3 mg oral: 39 mg–78 mg 6 mg oral: 117 mg 12 mg oral: 234 mg	$$$$$
Paliperidone palmitate (Invega Trinza) 2015	Schizophrenia (only after at least 4 months of adequate treatment on Invega Sustenna)	273, 410, 546, 819 mg in prefilled syringes	No overlap	3 months	Based on previous monthly Invega Sustenna dose: For 78 mg, give 273 mg Trinza For 117 mg, give 410 mg Trinza For 156 mg, give 546 mg Trinza For 234 mg, give 819 mg Trinza	Give same conversion dose of Trinza every 3 months; adjust if necessary per patient response	$$$$$
Risperidone (Perseris) 2018	Schizophrenia	90, 120 mg	No overlap	Monthly	Start 90 or 120 mg SQ to abdomen monthly	Approx. equivalence: 90 mg monthly: 3 mg/day oral 120 mg monthly: 4 mg/day oral	$$$$$
Risperidone (Risperdal Consta) 2003	Schizophrenia Bipolar, manic/mixed (monotherapy or adjunct)	12.5, 25, 37.5, and 50 mg vials	With usual oral dose for 21 days	2 weeks	Start at 25 mg Q2 weeks; adjust dose no more frequently than Q4 weeks as needed for response	Approx. equivalence: <4 mg/day oral: 25 mg 4 mg–6 mg/day oral: 37.5 mg >6 mg/day oral: 50 mg Maximum dose: 50 mg Q2 weeks	$$$$$

[1]brand discontinued; available as generic only

Table P4 Mean half-life and kinetic properties of commonly used long-acting injectable (LAI) antipsychotics [23–26]

Drug	Vehicle	Dosage	T_{max}	$T_{1/2}$ multiple dosing	Able to be loaded
First-generation antipsychotics					
Fluphenazine decanoate	Sesame oil	12.5–75 mg/2 weeks **Max:** 75 mg/week	0.3–1.5 days	14 days	Yes
Haloperidol decanoate	Sesame oil	25–300 mg/4 weeks **Max:** 300 mg/2 weeks	3–9 days	21 days	Yes
Perphenazine decanoate	Sesame oil	27–216 mg/3–4 weeks	7 days	27 days	Yes
Flupenthixol decanoate	Coconut oil	20–40 mg/2–4 weeks **Max:** 100 mg/2 weeks	4–7 days	17 days	Yes
Zuclopenthixol decanoate	Coconut oil	25–100 mg/2–4 weeks **Max:** 400 mg/2 weeks	3–7 days	19 days	Yes
Newer antipsychotics					
Risperidone subcutaneous **(Perseris®)**	Water	90–120 mg/4 weeks	7–8 days	9–11 days	Not needed
Risperidone microspheres **(Risperdal Consta®)**	Water	12.5–50 mg/2 weeks	21 days	See note [a]	**No** (21–28 days oral overlap)
Paliperidone palmitate **(Invega Sustenna®)**	Water	39–234 mg/4 weeks	13 days	25–49 days	Yes
Paliperidone palmitate (3 mo) **(Invega Trinza®)**[b]	Water	273–819 mg/12 weeks	84–95 days (deltoid) 118–139 days (gluteal)	30–33 days	No

Drug	Vehicle	Dosage	T_{max}	$T_{1/2}$ multiple dosing	Able to be loaded
Olanzapine pamoate (Zyprexa Relprevv®)	Water	150–300 mg/2 weeks 300–405 mg/4 weeks	7 days	30 days	Yes
Aripiprazole monohydrate (Abilify Maintena®)	Water	300–400 mg/4 weeks	6.5–7.1 days	29.9–46.5 days	No (14 days oral overlap)
Aripiprazole lauroxil (Aristada®)[c]	Water	441 mg, 662 mg, 882 mg/4 wks 882 mg/6 weeks 1064 mg/8 weeks	41 days (single dose) [27] 24.4–35.2 days (repeated dosing) [28]	53.9–57.2 days	No (Start with AL_{NC} 675 mg IM + 30 mg oral *OR* 21 days oral overlap)
Aripiprazole lauroxil nanocrystal (Aristada Initio®)[d]	Water	675 mg once	27 days (range: 16 to 35 days)	15–18 days (single dose)	–

[a] Steady state plasma levels after 5 biweekly injections are maintained for 4–5 weeks, but decrease rapidly at that point with a mean half-life of 4–6 days [29].
[b] Only for those on paliperidone palmitate monthly for 4 months. Cannot be converted from oral medication.
[c] Requires 21 days oral overlap unless starting with aripiprazole lauroxil nanocrystal (AL_{NC}) + a single 30 mg oral dose.
[d] Aripiprazole lauroxil nanocrystal (AL_{NC}) is only used for initiation of treatment with aripiprazole lauroxil, or for resumption of treatment. It is always administered together with the clinician-determined dose of aripiprazole lauroxil, although the latter can be given up to 10 days after the aripiprazole lauroxil nanocrystal (AL_{NC}) injection.

For further reading about use of LAI antipsychotics, please see the comprehensive edited book ***Antipsychotic Long-Acting Injections***, now in its 2nd edition [30].

Olantsapiinin aloitus:

2021 Maudsley Prescribing Guidelines

Table 1.5 Dosing schedules

Oral olanzapine equivalent	Loading dose	Maintenance dose (given 8 weeks after the first dose)
10mg/day	210mg every 2 weeks or 405mg every 4 weeks	300mg/4 weeks (or 150mg every 2 weeks)
15mg/day	300mg every 2 weeks	405mg/4 weeks (or 210mg every 2 weeks)
20mg/day	None – give 300mg every 2 weeks	300mg every 2 weeks

Risperidoni-ekvivalentit annokset:

2021 Maudsley Prescribing Guidelines

Approximate equivalent doses (mg)[10]

Risperidone oral (daily)	Risperdal Consta (2-weekly)	Paliperidone palmitate (monthly)	RBP-7000 (monthly)
2	25	50	Not available*
3	37.5	75	90
4	50	100	120
6	Not available	150	Not available

*Laffont et al.[11] suggest 90mg is equivalent to 25mg/2-weekly Risperdal Consta

Switching to aripiprazole LAI

Switching from	Aripiprazole LAI regimen
Oral antipsychotics	Cross taper antipsychotic with oral aripiprazole* over two weeks **One-injection start** Start aripiprazole LAI, continue aripiprazole oral for another two weeks and then stop **Two-injection start** Start aripiprazole LAI as indicated above after two weeks of oral aripiprazole, then stop oral treatment**.
Depot antipsychotics (not risperidone LAI)	Start oral aripiprazole* on day the last depot injection was due **One-injection start** Start aripiprazole LAI after two weeks and then stop oral aripiprazole two weeks later **Two-injection start** Start aripiprazole LAI as indicated above after two weeks of oral aripiprazole, then stop oral treatment**.
Risperidone LAI	Start oral aripiprazole* 4–6 weeks after the last risperidone injection **One-injection start** Start aripiprazole LAI two weeks later; discontinue oral aripiprazole two weeks after that **Two-injection start** Start aripiprazole LAI as indicated above after two weeks of oral aripiprazole, then stop oral treatment**.

*If prior response and tolerability to aripiprazole are known, pre-injection oral aripiprazole may not be strictly required. However, attainment of effective aripiprazole plasma levels is dependent upon four weeks of oral supplementation for the one-injection start regimen. Similarly, for the two-injection start regimen, the pharmacokinetic modelling study was based on plasma levels from oral aripiprazole being at steady state on the day of initiation.

**If oral aripiprazole cannot be given at all (e.g. patient refusal), always use the two-injection starting regimen. This 800mg dose is likely to afford therapeutic plasma concentrations even in the absence of prior oral treatment.

Risperidoni-aloitus:

2021 Maudsley Prescribing Guidelines

Table 1.10 Switching to risperidone long-acting injection (RLAI)

Switching from	Recommended method of switching	Comments
No treatment (new patient or recently non-compliant)	Start risperidone oral at 2mg/day and titrate to effective dose. If tolerated, prescribe equivalent dose of RLAI Continue with oral risperidone for at least 3 weeks then taper over 1–2 weeks. Be prepared to continue oral risperidone for longer	Use oral risperidone before giving injection to assure good tolerability Those stabilised on 2mg/day start on 25mg/2 weeks Those on higher doses, start on 37.5mg/2 weeks and be prepared to use 50mg/2 weeks (Manufacturer advice may differ from this – our guidance is based on numerous studies of dose-related outcome and on comparative plasma levels)

Xeplion-aloitus:

2021 Maudsley Prescribing Guidelines

Table 1.6 Paliperidone dose and administration information[2]

	Dose	Route
Initiation		
Day 1	150mg IM	Deltoid only
Day 8 (± 4 days)	100mg IM	Deltoid only
Maintenance		
Every month (± 7 days) thereafter	50–150mg IM*	Deltoid or Gluteal**

*The maintenance dose is perhaps best judged by consideration of what might be a suitable dose of oral risperidone and then giving paliperidone palmitate in an equivalent dose (see Table 1.7). Pre-treatment with oral risperidone is helpful in establishing efficacy and tolerability of a given dose.

**Continuation with deltoid injections for the first 6 months may be considered in some patients who switch from higher doses of oral paliperidone or risperidone.[2]

Xeplion-aloitus:

2021 Maudsley Prescribing Guidelines

Table 1.8 Switching to paliperidone palmitate 1-monthly LAI

Switching from	Recommended method of switching	Comments
No treatment	Give the two initiation doses: 150mg IM deltoid on day 1 and 100mg IM deltoid on day 8 Maintenance dose starts 1 month later	The manufacturer recommends a dose of 75mg monthly for the general adult population.[17] This is approximately equivalent to 3mg/day oral risperidone. (see Table 1.7). In practice, the modal dose is 100mg/month[18] Maintenance dose adjustments should be made monthly. However, the full effect of the dose adjustment may not be apparent for several months[2]
Oral paliperidone/ risperidone	Give the two initiation doses followed by the maintenance dose (See Table 1.7 and prescribe equivalent dose)	Oral paliperidone/risperidone supplementation during initiation is not necessary
Oral antipsychotics	Reduce the dose of the oral antipsychotic over 1–2 weeks following the first injection of paliperidone. Give the two initiation doses followed by the maintenance dose	

Xeplion-aloitus:

2021 Maudsley Prescribing Guidelines

Depot antipsychotic	Start paliperidone (at the maintenance dose) when the next injection is due. NB. No initiation doses are required	Doses of paliperidone palmitate IM are difficult to predict from the dose of FGA depots. The manufacturer recommends a dose of 75mg monthly for the general adult population but in practice 100mg and 150mg are more often prescribed.[18] If switching from risperidone LAI see Table 1.7 and prescribe equivalent dose Maintenance dose adjustments should be made monthly. However, the full effect of the dose adjustment may not be apparent for several months[2]
Antipsychotic polypharmacy with depot	Start paliperidone (at the maintenance dose) when the next injection is due. NB. No initiation doses are required Reduce the dose of the oral antipsychotic over 1–2 weeks following the first injection of paliperidone	Aim to treat the patient with paliperidone palmitate IM as the sole antipsychotic. The maintenance dose should be governed as far as possible by the total dose of oral and injectable antipsychotic (see dose equivalence table in this chapter)

Xeplion-Trevicta-siirtyminen:

2021 Maudsley Prescribing Guidelines

Table 1.9 Dosing of paliperidone LAI 3-monthly

Dose of paliperidone LAI 1-monthly	Dose of paliperidone LAI 3-monthly
50mg	175mg
75mg	263mg
100mg	350mg
150mg	525mg

See manufacturer's information for full information in missed doses.

LAI-aloitus ARIP-PALIPER-RISP:

2021 Maudsley Prescribing Guidelines

Newer long-acting injectable antipsychotic preparations

The following table provides brief details of some newer LAI antipsychotic formulations.

Drug	Trade name	Formulation	Dosing interval	Site(s) of administration	Dosing information	Pre-mixing required	Pre-treatment with oral therapy essential*	Pre-treatment with oral therapy desirable**	Regulatory status	Additional information
Aripiprazole lauroxil extended-release injectable	Aristada Initio	Nanocrystalline dispersion;[1] LinkeRx technology[2]	Single dose	Intra-muscular injection into the deltoid or gluteal muscle	675mg (IM dispersion = 459mg aripiprazole)[3]	No	Yes – but see additional information	Yes	FDA approved 2018[4]	Aristada initio, together with one 30mg dose of oral aripiprazole, is designed to only be given to initiate treatment with Aristada (see Aripiprazole LAI section in Chapter 1) and should not be used for repeated dosing.[5]
Paliperidone palmitate 6-month formulation	N/A	Micro-crystalline suspension	6-monthly	Intra-muscular injection	700mg/ 1000mg?[6]	No	No	No – patients will already have received long-acting paliperidone	Phase 3 study underway[7]	Designed for patients stabilised on PP1M or PP3M[8]
Risperidone for sub-cutaneous injection (RBP-7000)	Perseris	Suspension, Co-polymer; ATRIGEL technology[3]	1-monthly	Abdominal sub-cutaneous injection only[9]	90mg/120mg	Yes	No[10]	Yes	FDA approved 2018[11]	Does not require loading doses or oral supplementation. Prior tolerability with oral risperidone should be established[9]

(Continued)

LAI-aloitus ARIP-PALIPER-RISP:

2021 Maudsley Prescribing Guidelines

Drug	Trade name	Formulation	Dosing interval	Site(s) of administration	Dosing information	Pre-mixing required	Pre-treatment with oral therapy essential*	Pre-treatment with oral therapy desirable**	Regulatory status	Additional information
Risperidone extended release for SC injection (TV-46000)	N/A	Suspension	1- and 2- monthly[12]	Sub-cutaneous injection	2 dose regimens (TV-46000-A & TV-46000-B) being investigated[13]	No[12]	No[13]	Yes[13]	Phase 3 study in progress[13]	Phase 3 results are awaited in 2020[12]
Risperidone	Risperidone ISM or Doria	Suspension[14]	1-monthly[14]	Intra-muscular injection into the gluteal or deltoid muscle[15]	75mg/100mg	Yes	No[16]	Yes	Phase 3 study completed Awaiting EMA approval 2020[17]	Does not require loading doses or oral supplementation/3-day trial of oral risperidone (2mg/day) to check for hypersensitivity in risperidone naïve patients[18]

*LAI tested only in the presence of pre/post-treatment with oral therapy
**Best practice in order to establish efficacy and tolerability

LAI-vieroitusoireet , jos injektio jää ottamatta:

2021 Maudsley Prescribing Guidelines

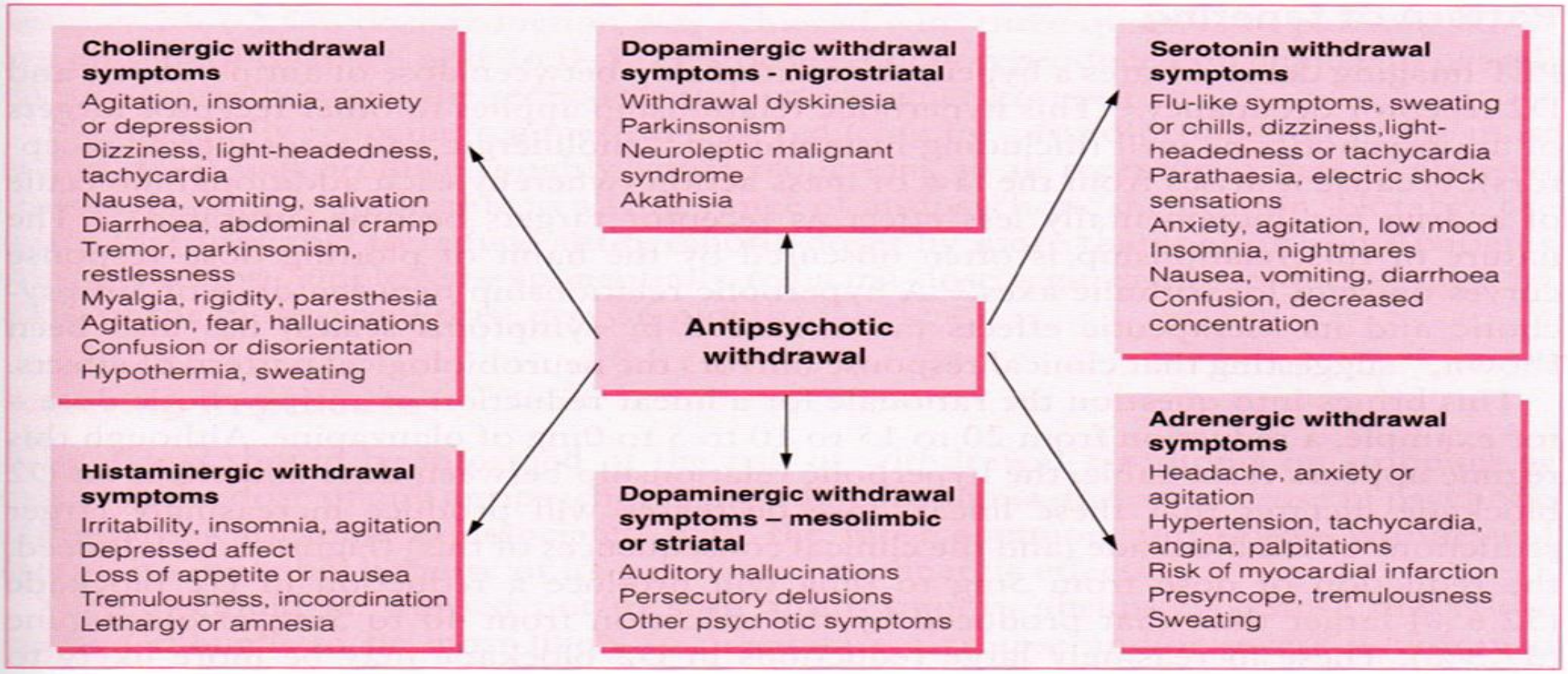


Figure 1.1 Antipsychotic withdrawal symptoms adapted from Chouinard et al. (2017)[11]

LAI-EPS (EP-oireet) : AP vaihto

2021 Maudsley Prescribing Guidelines

Switching antipsychotics

Summary of recommendations for switching antipsychotics because of poor tolerability.

Adverse effect	Suggested drugs	Alternatives
Acute EPS[1–8] Dystonia, parkinsonism, bradykinesia	Aripiprazole Brexpiprazole Cariprazine Olanzapine Quetiapine	Clozapine Lurasidone Ziprasidone
Akathisia[2,9,10]	Olanzapine Quetiapine	Clozapine Brexpiprazole
Dyslipidaemia[7,8,11–16]	Amisulpride Aripiprazole§ Lurasidone Ziprasidone	Asenapine Brexpiprazole Cariprazine
Impaired glucose tolerance[7,8,15,17–21]	Amisulpride Aripiprazole§ Lurasidone Ziprasidone	Brexpiprazole Cariprazine Haloperidol

LAI-EPS (EP-oireet) : AP vaihto

2021 Maudsley Prescribing Guidelines

Hyperprolactinaemia[7,8,15,22–28]	Aripiprazole§ Brexpiprazole Cariprazine Lurasidone Quetiapine	Clozapine Olanzapine Ziprasidone
Postural hypotension[8,15,29]	Amisulpride Aripiprazole Brexpiprazole Cariprazine Lurasidone	Haloperidol Sulpiride Trifluoperazine
QT prolongation[27,30–37]	Brexpiprazole Cariprazine Lurasidone Paliperidone	Low dose monotherapy of any drug not formally contra-indicated in QT prolongation (with ECG monitoring)
Sedation[7,8,27]	Amisulpride Aripiprazole Brexpiprazole Cariprazine Risperidone Sulpiride	Haloperidol Trifluoperazine Ziprasidone

(Continued)

LAI-EPS (EP-oireet) : AP vaihto

2021 Maudsley Prescribing Guidelines

(*Continued*)

Adverse effect	Suggested drugs	Alternatives
Sexual dysfuction[8,38–44]	Aripiprazole Brexpiprazole Cariprazine Lurasidone Quetiapine	Clozapine
Tardive dyskinesia[45–49]	Clozapine	Aripiprazole Olanzapine Quetiapine
Weight gain[16,35,37,50–57]	Amisulpride Aripiprazole§ Brexpiprazole Cariprazine Haloperidol Lurasidone Ziprasidone	Asenapine Haloperidol Trifluoperazine

§There is evidence that both switching to and co-prescription of aripiprazole can be associated with reductions in body weight and plasma prolactin levels, better lipid profiles, and a decrease in plasma glucose levels.[58–61]

LAI-EPS (EP-oireet) :

2021 Maudsley Prescribing Guidelines

Table 1.14 Most common extrapyramidal symptoms

	Dystonia (uncontrolled muscular spasm)	**Pseudoparkinsonism (bradykinesia, tremor, etc.)**	**Akathisia (restlessness)[16]**	**Tardive dyskinesia (abnormal involuntary movements)**
Signs and symptoms[17]	Muscle spasm in any part of the body, e.g. ▪ Eyes rolling upwards (oculogyric spasm) ▪ Head and neck twisted to the side (torticollis) The patient may be unable to swallow or speak clearly. In extreme cases, the back may arch or the jaw dislocate Acute dystonia can be both painful and very frightening	▪ Tremor and/or rigidity ▪ Bradykinesia (decreased facial expression, flat monotone voice, slow body movements, inability to initiate movement) ▪ Bradyphrenia (slowed thinking) ▪ Salivation Pseudoparkinsonism can be mistaken for depression or the negative symptoms of schizophrenia	A subjectively unpleasant state of inner restlessness with a desire or compulsion to move[1] ▪ Foot stamping when seated ▪ Constantly crossing/uncrossing legs ▪ Rocking from foot to foot ▪ Constantly pacing up and down Akathisia can be mistaken for psychotic agitation and has been linked with suicidal ideation[18] and aggression towards others[19]	A wide variety of movements can occur,[20] such as: ▪ Lip smacking or chewing ▪ Tongue protrusion ('fly catching') ▪ Choreiform hand movements ('piano playing') ▪ Dystonic and choreoathetoid movements of the limbs Severe orofacial movements can lead to difficulty speaking, eating or breathing. Movements are worse when under stress.
Rating scales	No specific scale. Small component of general EPS scales	Simpson–Angus EPS Rating Scale[21]	Barnes Akathisia Rating Scale[22]	Abnormal Involuntary Movement Scale[23] (AIMS)
Prevalence	Approximately 10%,[24] but more common:[25] ▪ In young males ▪ In those who are antipsychotic-naive ▪ With high potency medications (e.g. haloperidol) Dystonic reactions are rare in the elderly	Approximately 20%,[26] but more common in: ▪ Elderly females ▪ Those with pre-existing neurological damage (head injury, stroke, etc.)	Wide variation but approximately 25%[27] for acute akathisia with FGAs, lower with SGAs The relative liability of individual antipsychotic medications for akathisia is uncertain,[28] but there is consensus that the incidence is lowest for olanzapine, quetiapine and clozapine.[29,30]	5% of patients per year of antipsychotic exposure.[31] More common in respect to:[32] ▪ Age ▪ Affective illness ▪ Schizophrenia ▪ Higher doses ▪ Acute EPS early in treatment Lower incidence in those on SGAs[33] TD may be associated with neurocognitive deficits.[34]

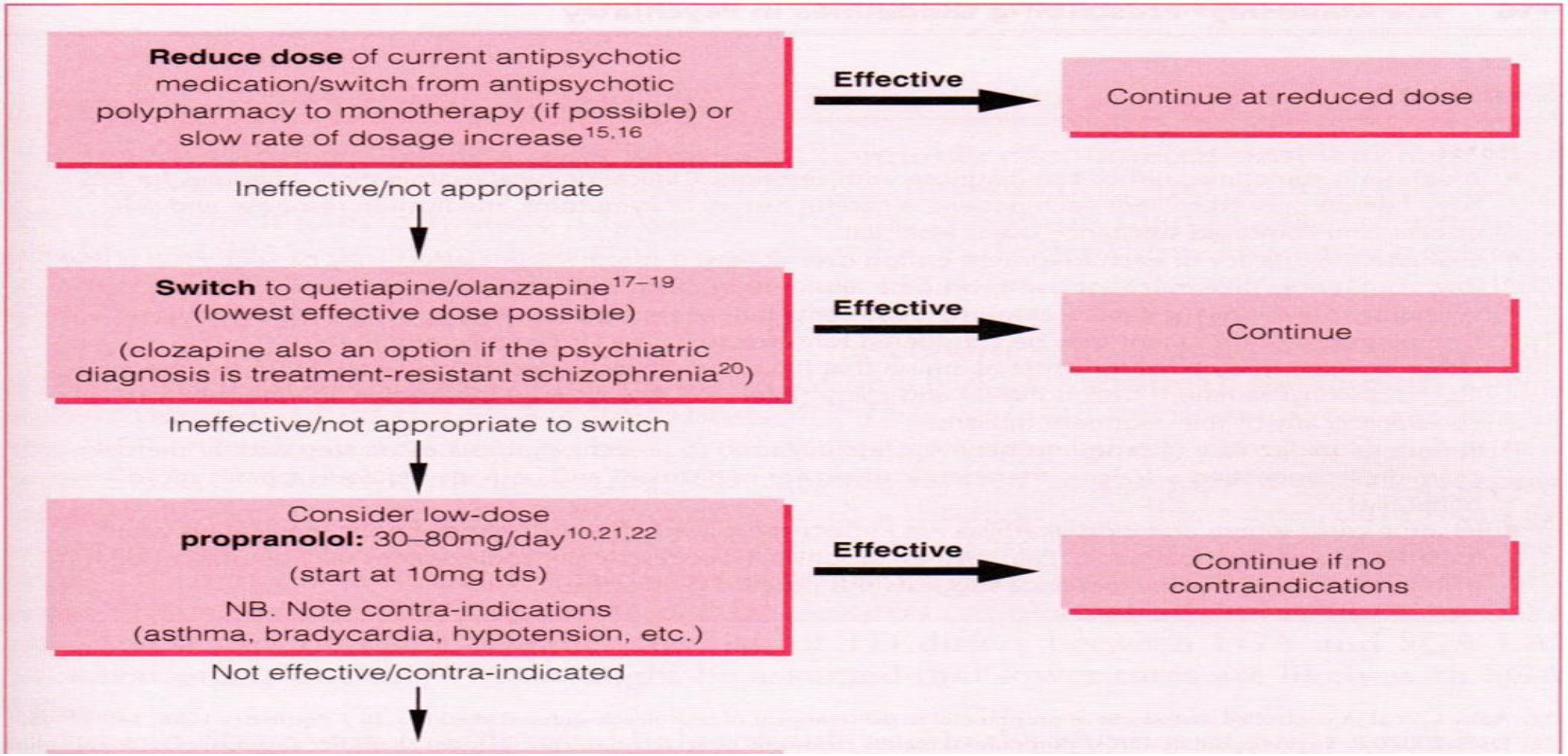
LAI-EPS (EP-oireet) : jatkuu

2021 Maudsley Prescribing Guidelines

	Dystonia (uncontrolled muscular spasm)	Pseudoparkinsonism (bradykinesia, tremor, etc.)	Akathisia (restlessness)[16]	Tardive dyskinesia (abnormal involuntary movements)
Time taken to develop	Acute dystonia can occur within hours of starting antipsychotic medication (minutes if the IM or IV route is used). Tardive dystonia occurs after months to years of antipsychotic treatment.	Days to weeks after antipsychotic medication is started or the dose is increased	Acute akathisia occurs within hours to weeks of starting antipsychotic medication or increasing the dose. Akathisia that has persisted for several months or so is called 'chronic akathisia'. Tardive akathisia tends to occur later in treatment and may be exacerbated or provoked by antipsychotic dose reduction or withdrawal.[16]	Months to years The proportion of cases showing reversibility on cessation of antipsychotic medication is unclear and may partly depend on age[20]
Treatment	Anticholinergic drugs given orally, IM or IV depending on the severity of symptoms[20] ▪ Remember the patient may be unable to swallow ▪ Response to IV administration will be seen within 5 minutes ▪ Response to IM administration takes around 20 minutes ▪ Tardive dystonia may respond to ECT[35,36] ▪ Where severe symptoms do not respond to simpler measures including switching to an antipsychotic with a low propensity for EPS, botulinum toxin may be effective[37,38]	Several options are available depending on the clinical circumstances: ▪ Reduce the antipsychotic dose ▪ Change to an antipsychotic medication with a lower propensity for pseudoparkinsonism (see section on relative liability of antipsychotic medications for adverse effects) ▪ Prescribe an anticholinergic. The majority of patients do not require long-term anticholinergic agents. Use should be reviewed at least every 3 months. Do not prescribe at night (symptoms usually absent during sleep)	▪ Reduce the antipsychotic dose ▪ Change to an antipsychotic drug with lower propensity for akathisia (see sections on akathisia and relative liability of antipsychotic medications for adverse effects) ▪ A reduction in symptoms may be seen with:[39–41] low-dose propranolol, 30–80mg/day, clonazepam (low dose), $5HT_2$ antagonists such as: cyproheptadine,[36] mirtazapine,[40] trazodone,[42,43] mianserin,[44] and cyproheptadine[36] may help, as may possibly diphenhydramine.[45] All are unlicensed for this indication Anticholinergics are generally unhelpful unless akathisia is part of a general EPS spectrum[46]	▪ Stop anticholinergic if prescribed ▪ Reduce dose of antipsychotic medication ▪ Change to an antipsychotic with lower propensity for TD,[47–50] note that data are conflicting.[51,52] ▪ Clozapine is the antipsychotic most likely to be associated with resolution of symptoms.[53,54] Quetiapine may also be useful in this regard.[55] ▪ Both valbenazine and deutetrabenazine have a positive risk-benefit balance as add-on treatments[53,56–60] ▪ There is also some evidence for tetrabenazine and ginkgo biloba[61] as add-on treatments. For other treatment options[60,62] the review by the American Academy of Neurology[63] and the section on tardive dyskinesia

LAI-EPS – akatitisia:

2021 Maudsley Prescribing Guidelines



LAI-EPS – akatitisia:

2021 Maudsley Prescribing Guidelines

(Continued)

LAI-EPS – akatitisia:

2021 Maudsley Prescribing Guidelines

(*Continued*)

Notes

- Akathisia is sometimes difficult to diagnose with certainty. Clinical physical examination schedules for EPS have been proposed.[30,31] For each patient, a careful history of symptoms, medication response and side effects, and comorbid substance use is essential.
- Evaluate the efficacy of each treatment option over at least 1 month. Some effect may be seen after a few days, but it may take much longer to become apparent in those with chronic akathisia.
- Withdraw previously ineffective akathisia treatments before starting the next option in the algorithm.
- Combinations of treatment may be considered for refractory cases if carefully monitored.
- Other possible treatments for acute akathisia that have been investigated include vitamin B6,[32,33] pregabalin,[34] diphenhydramine,[35] trazodone[23,36] and zolmitriptan.[37,38] Always read the primary literature before considering any of the treatment options.
- Parenteral midazolam (1.5mg) has been successfully used to prevent akathisia associated with IV metoclopramide,[39] suggesting a specific therapeutic effect for midazolam and perhaps benzodiazepines more generally.
- In some cases where agitation/akathisia are known short-lived effects of antipsychotic medication when initiated (e.g. with aripiprazole, cariprazine), prophylactic or rescue benzodiazepines may be prescribed for a limited period. Clinical experience suggests this practice is effective.

LAI-EPS – TD:

2021 Maudsley Prescribing Guidelines

Table 1.15 First-choice agents (alphabetical order; no preference implied)

Drug	Comments
Amantadine[49–52]	Rarely used but apparently effective at 100–300mg a day
Benzodiazepines[32,33]	Widely used for TD, but Cochrane review considered that the limited evidence for efficacy is inconclusive.[53] Intermittent use may be necessary to avoid tolerance to effects. Most commonly used are clonazepam 1–4mg/day and diazepam 6–25mg/day, with better supporting evidence for the former[36,54]
Deutetrabenazine[8,52,55–57]	Deutetrabenazine (VMAT-2 inhibitor) is also effective as a treatment for TD. Licensed for TD in the USA.[58] Better supporting evidence than for tetrabenazine. Longer half-life than tetrabenazine but still needs to be taken twice a day. Low incidence of psychiatric and neurological effects. Dose is 12–48mg/day
Ginkgo biloba[52,59]	Well tolerated. Cochrane review concluded that while Ginkgo biloba could reduce TD symptoms, the available evidence did not justify its routine use as a treatment.[60] A meta-analysis of three Chinese RCTs showed a good effect with 240mg/day[61]
Pyridoxine[62]	Supported by Cochrane[63] and a meta-analysis.[49] Dose – up to 400mg/day
Tetrabenazine[64,65]	Only licensed treatment for moderate to severe TD in UK. Depression, drowsiness, parkinsonism and akathisia may occur.[54,66] Dose is 25–200mg/day. Reserpine (similar mode of action) also effective but rarely, if ever, used
Valbenazine[8,56,60,67–70]	The evidence supports a favourable benefit-risk ratio for valbenazine (VMAT-2 inhibitor) as a treatment for TD. Licensed for TD in the USA.[71] A dose of 80mg once daily is effective with a benign cardiovascular profile. Low incidence of depression and akathisia
Vitamin E[49,72]	Numerous studies but efficacy remains to be conclusively established. Cochrane suggest that there is evidence only for slowing deterioration of TD.[8,73] Dose is in the range 400–1600 IU/day

LAI-EPS – TD: jatkuu

2021 Maudsley Prescribing Guidelines

Table 1.16 Other options for the treatment of TD

Drug	Comments
Amino acids[74]	Use is supported by a small randomised, placebo-controlled trial. Low risk of toxicity
Botulinum toxin[75–78]	Case reports of success for localised dyskinesia. Probably now treatment of choice for disabling or distressing focal symptoms
Calcium antagonists[79]	A few published studies but not widely used. Cochrane is dismissive.[80] A meta-analysis found no effect[49]
Donepezil[81–83]	Supported by a single open study and case series. One negative RCT (n = 12). Dose is 10mg/day. No clear evidence of efficacy for rivastigmine or galantamine[84]
Fish oils[85,86]	Very limited support for the use of EPA at dose of 2g/day
Fluvoxamine[87]	Three case reports. Dose is 100mg/day. Beware of interactions
Gabapentin[88]	Adds weight to theory that GABAergic mechanisms improve TD. Dose is 900–1200mg/day. Inconclusive data on other GABA agonists[89]
Levetiracetam[90–93]	Three published case studies. One RCT. Dose up to 3000mg/day
Melatonin[94]	Use is supported by a meta-analysis of four trials.[95] Usually well tolerated. Dose is 10mg/day. Some evidence that melatonin receptor genotype determines risk of TD[96]
Naltrexone[97]	May be effective when added to benzodiazepines. Well tolerated. Dose is 200mg/day
Ondansetron[98,99]	Limited evidence but low toxicity. Dose – up to 12mg/day
Propranolol[100–102]	Formerly a relatively widely used treatment. Open-label studies only and a prospective randomized trial is probably warranted. Dose is 40–120mg/day. Beware of contra-indications (asthma, bradycardia, hypotension)
Quercetin[103]	Plant compound which is thought to be an antioxidant. Some promising case reports[103–105]
Sodium oxybate[106]	One case report. Dose was 8g/day
Repetitive transcranial magnetic stimulation (rTMS)[107,108]	RCT data on patients with 'tardive syndromes' suggest the potential for bilateral hemispheric high frequency rTMS to be a feasible treatment where TD is unresponsive to 'first-line' medical treatment[107]
Zolpidem[109]	Three case reports. Dose 10–30mg a day

LAI-EPS – painonnousu

2021 Maudsley Prescribing Guidelines

Table 1.17 Antipsychotic-induced weight gain[18–25]

Drug	Risk/extent of weight gain
Clozapine	**High**
Olanzapine	
Chlorpromazine	**Moderate**
Iloperidone	
Sertindole	
Quetiapine	
Risperidone	
Paliperidone	
Amisulpride	**Low**
Asenapine	
Brexpiprazole	
Aripiprazole	
Cariprazine	
Haloperidol	
Lumateperone	
Lurasidone	
Sulpiride	
Trifluoperazine	
Ziprasidone	

LAI-EPS – painonnousu th

2021 Maudsley Prescribing Guidelines

Table 1.18 *(Continued)*

Drug	Comments
Metformin[2,32,53,54] (500–2000mg/day)	Now a substantial database (in non-diabetic patients) supporting the use of metformin in both reducing and reversing weight gain caused by antipsychotics (mainly olanzapine). Beneficial effects on other metabolic parameters. Some negative studies, but clear and significant effect in meta-analyses. One positive RCT[55] and extension study[56] in children and adolescents with ASD published since then. Ideal for those with weight gain and diabetes or polycystic ovary syndrome. Note that metformin treatment increases the risk of vitamin B_{12} deficiency[57]
Melatonin[58–60] (up to 5mg at night)	One small RCT showing attenuation of olanzapine-induced weight gain. Other studies show negative results. Effect, if any, is small
Methylcellulose (1,500mg ac)	Old-fashioned and rather unpalatable preparation. No data in drug-induced weight gain but once fairly widely used. Also acts as a bulk-forming laxative, so may be suitable for clozapine-related weight gain
Modafinil[61,62] (up to 300mg/day)	Limited positive data and one negative RCT for clozapine-induced weight gain. Not recommended
Naltrexone[63,64] (25–50mg/day)	Some positive results but evidence is limited to two small pilot RCTs. Not recommended

LAI-EPS – painonnousu th

2021 Maudsley Prescribing Guidelines

Orlistat[65–70] (120mg tds ac/pc)	Reliable effect in obesity, especially when combined with calorie restriction. Few published data in medication-induced weight gain but widely used in practice with some success. In trials for clozapine or olanzapine-induced weight gain effect was only seen for men.[69,70] When used without calorie restriction in psychiatric patients, the effects are very limited. Failure to adhere to a low-fat diet will result in fatty diarrhoea and possible malabsorption of orally administered medication. Overall, a good choice for clozapine-induced weight gain where it reduces both weight and the incidence of constipation[71]
Reboxetine[15] (4–8mg daily)	Attenuates olanzapine-induced weight gain. Reverses some metabolic changes.[72] Effective when combined with betahistine
Topiramate[32,54,73,74] (Up to 300mg daily)	Reliably reduces weight even when medication-induced. Meta-analyses of RCTs suggest a greater effect for prevention rather than treatment. Problems may arise because of topiramate's propensity for causing sedation, confusion and cognitive impairment. May have antipsychotic properties
Zonisamide[75] (100–600mg/day)	Antiepileptic drug with weight reducing properties. A RCT of 150mg a day showed significant weight reduction in people receiving SGAs. Another RCT (up to 600mg/day) shows attenuated olanzapine-induced weight gain. Sedation, diarrhoea and cognitive impairment are the most common problems. Not recommended

ac, ante cibum (before meals); ASD, autism spectrum disorders. bd, bis in die (twice a day); pc, post cibum (after meals); tds, ter die sumendum (three times a day)

LAI-EPS – NMS

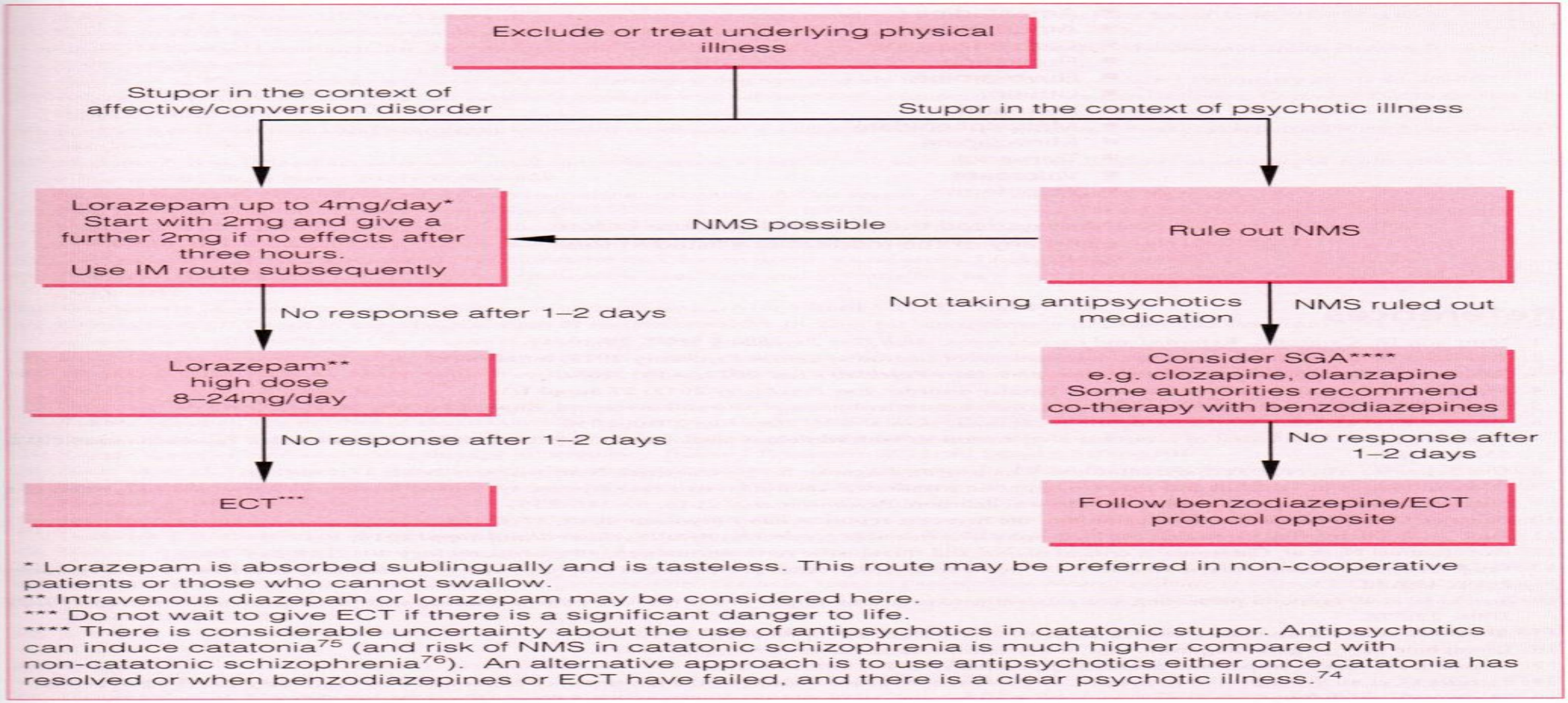
2021 Maudsley Prescribing Guidelines

Table 1.19 Neuroleptic malignant syndrome

Signs and symptoms[9,51–53] (presentation varies considerably)[54]	Fever, diaphoresis, rigidity, confusion, fluctuating level of consciousness. Fluctuating blood pressure, tachycardia Elevated creatine kinase, leukocytosis, altered liver function tests
Risk factors[8,11,48,52,53,55–57]	High-potency FGAs, recent or rapid dose increase, rapid dose reduction, abrupt withdrawal of anticholinergic agents, antipsychotic polypharmacy Psychosis, organic brain disease, alcoholism, Parkinson's disease, hyperthyroidism, psychomotor agitation, mental retardation Male gender, younger age Agitation, dehydration
Treatments[9,52,58–60] (guideline recommendations for NMS treatment are heterogeneous and based on limited evidence[47])	**In the psychiatric unit:** Withdraw antipsychotic medication, monitor temperature, pulse, BP. Consider benzodiazepines if not already prescribed – IM lorazepam has been used[61] **In the medical/A&E unit:** Rehydration, bromocriptine + dantrolene, sedation with benzodiazepines, artificial ventilation if required L-dopa, apomorphine, and carbamazepine have also been used, among many other drugs. ECT may be effective for NMS, even after pharmacotherapy has failed[62,63]
Restarting antipsychotics[41,52,58,64]	Antipsychotic treatment will be required in most instances and re-challenge is associated with acceptable risk Stop antipsychotic medication for at least 5 days, preferably longer. Allow time for symptoms and signs of NMS to resolve completely Begin with very small dose and increase very slowly with close monitoring of temperature, pulse and blood pressure. CK monitoring may be used but is controversial.[53,65] Close monitoring of physical and biochemical parameters is effective in reducing progression to 'full-blown' NMS[66,67] Consider using an antipsychotic medication structurally unrelated to that previously associated with NMS or a drug with low dopamine affinity (quetiapine or clozapine). Aripiprazole may also be considered,[68] but it has a long plasma half-life and has been linked to an increased risk of NMS[11] Avoid depot/LAI antipsychotic preparations (of any kind) and high potency FGAs

LAI-EPS – katatonia

2021 Maudsley Prescribing Guidelines



LAI-EPS – katatonia th muu kuin bdz

2021 Maudsley Prescribing Guidelines

Table 1.20 Medications other than benzodiazepines reported as treatments for catatonia/stupor

Listed in alphabetical order – no ranking or judgement is implied by the order

Antipsychotic medications[64–69,77–80]

- Aripiprazole
- Clozapine
- Olanzapine
- Risperidone
- Ziprasidone

Experimental treatments* [6,7,31,32,53,81–86]

- Amantadine
- Amitriptyline
- Carbamazepine
- Fluoxetine
- Fluvoxamine
- Lithium
- Memantine
- Methylphenidate
- Mirtazapine
- Tramadol
- Valproate
- Zolpidem

*Always read the primary literature before using any of the medications listed in this section.

LAI-EPS – QTc

2021 Maudsley Prescribing Guidelines

Table 1.21 Effects of antipsychotics on QTC[13,22,23,32–61].

No effect
Brexpiprazole*
Cariprazine*
Lurasidone
Lumateperone*

Low effect
Aripiprazole**
Asenapine
Clozapine
Flupentixol
Fluphenazine
Perphenazine
Prochlorperazine
Olanzapine***
Paliperidone
Risperidone
Sulpiride

Moderate effect
Amisulpride****
Chlorpromazine
Haloperidol
Iloperidone
Levomepromazine
Melperone
Pimavanserin
Quetiapine
Ziprasidone

High effect
Any intravenous antipsychotic
Pimozide
Sertindole
Any drug or combination of drugs used in doses exceeding recommended maximum

Unknown effect
Loxapine
Pipotiazine
Trifluoperazine
Zuclopenthixol

*Limited clinical experience (association with QT prolongation may emerge).
**One case of torsades de pointes (TDP) reported,[62] two cases of QT prolongation[63,64] and an association with TDP found in database study.[65] Healthy volunteer data suggest aripiprazole causes QTc prolongation of around 8ms.[66] Aripiprazole may increase QT dispersion.[67]
***Isolated cases of QTc prolongation[37,68] and has effects on cardiac ion channel, I_{Kr},[69] other data suggest no effect on QT_C.[23,35,36,70]
****TDP common in overdose,[25,71] strong association with TDP in clinical doses.[65]

LAI-EPS – QTc riskitekijät

2021 Maudsley Prescribing Guidelines

Table 1.22 Physiological risk factors for QTc prolongation and arrhythmia

Cardiac
Long QT syndrome
Bradycardia
Ischaemic heart disease
Myocarditis
Myocardial infarction
Left ventricular hypertrophy
Metabolic
Hypokalaemia
Hypomagnesaemia
Hypocalcaemia
Others
Extreme physical exertion
Stress or shock
Anorexia nervosa
Extremes of age – children and elderly may be more susceptible to QT changes
Female gender

Note: Hypokalaemia-related QTc prolongation is more commonly observed in acute psychotic admissions.[80] Also, be aware that there are a number of physical and genetic factors which may not be discovered on routine examination but which probably predispose patients to arrhythmia.[81,82]

LAI-EPS – QTc riskitekijät

2021 Maudsley Prescribing Guidelines

Table 1.23 Non-psychotropics associated with QT prolongation (see Crediblemeds.org for latest information)

Antibiotics Erythromycin Clarithromycin Ampicillin Co-trimoxazole Pentamidine (some four quinolones affect QTc – see manufacturers' literature)	**Antiarrhythmics** Quinidine Disopyramide Procainamide Sotalol Amiodarone Bretylium
Antimalarials Chloroquine Mefloquine Quinine	**Others** Amantadine Cyclosporin Diphenhydramine Hydroxyzine Methadone Nicardipine Tamoxifen

Note: β_2 agonists and sympathomimetics may provoke torsade de pointes in patients with prolonged QTc.

LAI-EPS – QTc EKG

2021 Maudsley Prescribing Guidelines

Table 1.24 Management of QT prolongation in patients receiving antipsychotic drugs

QTc	Action	Refer to cardiologist
<440ms (men) or <470ms (women)	None unless abnormal T-wave morphology	Consider if in doubt
>440ms (men) or > 470ms (women) but < 500ms	Consider reducing dose or switching to drug of lower effect; repeat ECG	Consider
>500ms	Repeat ECG. Stop suspected causative drug(s) and switch to drug of lower effect	Immediately
Abnormal T-wave morphology	Review treatment. Consider reducing dose or switching to drug of lower effect	Immediately

LAI-EPS – DM seulonta

2021 Maudsley Prescribing Guidelines

Table 1.25 Recommended monitoring for diabetes in patients receiving antipsychotic drug

Recommended monitoring	Ideally	Minimum
Baseline	OGTT or FPG HbA_{1C} if fasting not possible	Urine glucose (UG) Random plasma glucose (RPG)
Continuation	All drugs: OGTT or FPG + HbA_{1C} at 4–6 months then every 12 months. For clozapine and olanzapine or if other risk factors present: OGTT or FPG after one month, then every 4–6 months. For on-going regular screening, HbA_{1C} is a suitable test. Note that this test is not suitable for detecting short-term change.	UG or RPG every 12 months, with symptom monitoring

FPG, fasting plasma glucose; OGTT, oral glucose tolerance tests; RPG, random plasma glucose

Olantsapiinin vähennysohjelma:

2021 Maudsley Prescribing Guidelines

Table 1.11 Reductions of olanzapine dose by 5 percentage points of D2 occupancy at each step

Period	Olanzapine dose (mg)	D2 Occupancy (%)
1	20	81.6
2	14	75
3	10.5	70
4	8.4	65
5	6.8	60
6	5.5	55
7	4.5	50
8	3.7	45
9	3	40
10	2.4	35
11	1.9	30
12	1.5	25
13	1.1	20
14	0.8	15
15	0.5	10
16	0.24	5
17	0	0

Olantsapiinin vähennysohjelma:

2021 Maudsley Prescribing Guidelines

Table 1.12 Reductions of olanzapine dose by 2.5 percentage points of D2 occupancy at each step. Larger reductions that are 'evenly spaced' in terms of effect on D2 occupancy could be achieved by following every second or third step of this regimen

Period	Olanzapine dose (mg)	D2 occupancy (%)	Period	Olanzapine dose (mg)	D2 occupancy (%)
1	20	81.6	**18**	2.7	37.5
2	15.5	77.5	**19**	2.4	35
3	13.5	75	**20**	2.2	32.5
4	11.9	72.5	**21**	1.9	30
5	10.5	70	**22**	1.7	27.5
6	9.3	67.5	**23**	1.5	25
7	8.4	65	**24**	1.3	22.5
8	7.5	62.5	**25**	1.1	20
9	6.8	60	**26**	0.95	17.5
10	6.1	57.5	**27**	0.8	15
11	5.5	55	**28**	0.65	12.5
12	5	52.5	**29**	0.5	10
13	4.5	50	**30**	0.37	7.5
14	4.1	47.5	**31**	0.24	5
15	3.7	45	**32**	0.1	2.5
16	3.3	42.5	**33**	0	0
17	3	40			

Olantsapiinin vähennysohjelma:

2021 Maudsley Prescribing Guidelines

Table 1.13 A summary of potential reduction schedules for olanzapine

Reduce olanzapine by 5–10mg every 2–3 months until reaching 20mg per day, *then*

Reduce dose by 2.5–5mg every 2–3 months until reaching 10mg per day, *then*

Reduce dose by 1.25–2.5mg every 2–3 months until reaching 5mg per day, *then*

Reduce dose by 0.6–1.25mg every 2–3 months until reaching 2.5mg per day, *then*

Reduce dose by 0.3–0.6mg every 2–3 months until reaching 1.25mg per day, *then*

Reduce dose by 0.15–0.3mg every 2–3 months until reaching 0.6mg per day, *then*

Reduce dose by 0.07–0.15mg every 2–3 months until olanzapine is **completely stopped**.

This process should take 12–48 months, depending on how the patient tolerates the reductions.